PAIN-RELATED DISABILITY AMONG PEOPLE WITH CHRONIC OROFACIAL PAIN

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ABSTRACT

Vanessa Eve Miller: Pain-related Disability Among People with Chronic Orofacial Pain
(Under the direction of Gary Slade and Charles Poole)

High pain-related disability diminishes quality of life and increases health care costs. This study evaluated characteristics discriminating between high and low pain-related and examined the relationship between factors associated with pain-related disability among people with chronic painful temporomandibular disorder (TMD).

We conducted a cross-sectional analysis of a community-based sample of 1088 individuals with chronic TMD who completed standardized questionnaires assessing four domains: 1) sociodemographic, 2) psychological distress, 3) clinical pain, and 4) experimental pain. We used high pain-related disability, classified using the Graded Chronic Pain Scale, as the dependent variable in logistic regression modeling to evaluate contributions of variables from each domain. Cross-validated area under the ROC curve (AUC) quantified model discrimination.

We re-validated this measure of pain-related disability and created measurement models of TMD clinical features, psychological distress, and experimental pain sensitivity. Latent variables were combined for a full structural equation model that was crafted with exploratory model changes.

Participants were 18-44 years old (mean 29.2, SD ± 7.8) with a mean duration of 6.9 (6.4) years of chronic TMD. A third of participants had high pain-related disability. An 18-variable model encompassing all four domains had good discrimination (AUC=0.79 95% CI 0.75,0.82), as did a simplified model (sociodemographic variables plus catastrophizing, jaw limitation, and number of painful body sites: AUC=0.79 95% CI 0.76,0.82). Duration of pain, gender, and experimental pain testing results were not predictive.

Our structural equation model of pain-related disability, TMD features, and psychological distress was created and refined based on exploratory model revisions. Estimation of the final model indicated a good fit with the data. TMD clinical features and psychological distress predicted pain-related disability but experimental pain sensitivity did not. The final model explained 78% of the variance in pain-related disability.

High-impact chronic pain is a common problem among people with painful TMD. Assessment of characteristics associated with high-impact pain can be easily performed to identify modifiable risk factors and reduce high-impact pain. TMD clinical features (specifically jaw limitation) and psychological distress (including negative affect, somatization, and catastrophizing) should be considered by clinicians and researchers addressing pain-related disability.

I dedicate this work in loving memory of Epi Miller.

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I have been very fortunate to have the benefit of the support, wisdom and leadership of my primary mentor, Gary Slade, who encouraged me to apply to the PhD program and unfailingly mentored me every step of the way as I found my own footing. Throughout this arduous journey you have provided immeasurable guidance and opportunities, for which I will remain forever grateful. I would like to acknowledge the interdisciplinary group of collaborators I admire and was lucky enough to work with: Charles Poole, Yvonne Golightly, Ding-Geng Chen, and Deborah Barrett. Thank you for your time and thoughtful contributions to this work.

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may not have said to Christopher when we danced the merengue back at Antioch, I now say to the world, “Come at me”.

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LIST OF ABBREVIATIONS

AIC	Akaike information criterion
BIC	Bayesian information criterion
AUC	Area under the curve
CBT	Cognitive Behavior Therapy
CI	Confidence interval
CFI	Comparative fix index
CSQ	Coping Strategies Questionnaire
EM	Expectation maximum
GCPS	Graded Chronic Pain Scale
JFLS	Jaw Functional Limitation Scale
OBC	Oral Behavior Checklist
POMS-Bi	Profile of Mood States-Bipolar
RDC/TMD	Research Diagnostic Criteria for Temporomandibular Disorder
RMSEA	Root mean squared error of approximation
ROC	Receiver operating characteristic
SCL-90r	Symptom Checklist 90 revised
SD	Standard deviation
SE	Standard error
SEM	Structural equation model
SRMR	Standardized root mean residual
TLI	Tucker Lewis index
TMD	Temporomandibular Disorder

CHAPTER ONE: SPECIFIC AIMS

The goal of this study was to understand the epidemiology of pain-related disability (also called high-impact pain) among people with painful TMD. The approach was twofold: 1) to determine characteristics that could be used to distinguish between people with low or high pain-related disability and 2) examine relationships between factors associated with pain-related disability.

By studying the impact of pain, we seek to understand the experience of people with painful TMD while recognizing the decrease in quality of life and the increase in healthcare spending accompanying high pain-related disability. Identifying factors associated with high pain-related disability will be useful for clinicians predicting the trajectory of chronic orofacial pain and identifying patients at increased risk for disability. Once these characteristics are identified, they can be targeted in longitudinal research to understand the etiology of pain-related disability and treatment studies aiming to reduce pain-related disability. A reduction in high-impact pain among people with chronic pain would thereby considerably reduce the public health burden of pain. This is particularly important for people suffering from chronic pain with no available cure.

Aim 1: Explore associations between sociodemographic, psychological distress, clinical features, and experimental pain sensitivity domains and high pain-related disability among people with chronic TMD.

Hypothesis: Among people with chronic TMD, characteristics indicating more severe pain (such as decreased jaw opening limitation and increased pain sensitivity), increased psychological distress (high levels of anxiety and depression), additional comorbid conditions, and a lack of active coping strategies will allow discrimination between high and low pain-related disability.

Objective: Describe the prevalence of pain-related disability, distinguish between people with low or high pain-related disability, and determine factors associated with high pain-related disability.

Method: Perform binary logistic regression with the outcome variable of low or high pain-related disability. Use area under the receiver operator curve indicating sensitivity and specificity based on variables representing sociodemographic, psychological distress, clinical pain, and experimental pain domains to identify the simplest model with the highest AUC to discriminate between people with low or high pain-related disability.

Aim 2: Create and evaluate a structural equation model of pain-related disability in people with TMD with factors representing psychological distress, clinical TMD features, and experimental pain sensitivity.

Hypothesis: Pain-related disability is a multi-faceted construct that potentially involves psychological distress including catastrophizing and negative affect, clinical TMD features such as jaw opening, and biological pathology measured by experimental pain testing results.

Objectives: Addressing this aim requires three objectives: 1) re-validate the Graded Chronic Pain Scale for measuring pain-related disability with the inclusion of an item measuring

presenteeism, 2) create measurement models of latent constructs representing psychological distress, clinical TMD features, and experimental pain sensitivity, and 3) develop a well-fitting structural equation model quantifying the relationship between these latent variables while controlling for demographic variables.

Method: Use structural equation modeling including confirmatory factor analysis for the GCPS and measurement models for psychological distress, clinical TMD features, and experimental pain sensitivity. Evaluate factor loading onto latent variables representing pain-related disability to quantify the relationship between the latent structures.

CHAPTER TWO: BACKGROUND AND SIGNIFICANCE

Painful temporomandibular disorder (TMD) is a chronic pain condition that frequently co-occurs with other idiopathic chronic pain conditions involving a variety of bodily pain symptoms. Prevalence of TMD symptoms in U.S. adults was 5% in the 2009 National Health Interview Survey (NHIS). For people with TMD, average symptom ratings are consistent with mild to moderate levels of pain intensity. The Surgeon General's Report "Oral Health in America" (2000) declares, "Oral-facial pain… as a condition in and of itself, is a major source of diminished quality of life."

The diminished quality of life and pain-related disability resulting from painful TMD have been studied in a variety of ways including pain intensity, interference, functional limitation, oral behaviors, oral health quality of life, and activities of daily living. Although TMD is a localized pain condition, the pain frequently can result in interference and limitations in activities directly related to quality of life. This is why **the goals of this dissertation are to explore and define characteristics associated with high-impact pain among those with painful TMD**. This was accomplished with prediction modeling to describe characteristics associated with high-impact pain among chronic TMD cases and structural equation modeling of pain-related disability.

Pain-related disability (or high-impact pain) is a complex concept that is a unique measurement of the experience of living with chronic pain. These aims are both exploratory and hypothesis-testing aims designed to address the epidemiology of high-impact pain among people

with localized orofacial pain. Understanding pain impact as a unique factor that may influence functioning and progression of disease is very important for understanding the public health burden of painful TMD and other comorbid pain conditions that frequently occur in people with TMD.

Definitions of 'chronic pain'

The International Association for the Study of Pain (IASP) provides the most widely accepted description of pain:

> *An unpleasant **sensory** and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. . . . Pain is always subjective. . . . It is unquestionably a sensation in a part or parts of the body, but it is also always unpleasant and therefore also an **emotional** experience*[1]. (emphasis added)

This definition includes the important components of sensory and emotional experiences but do not speak to any functional involvement either as an outcome or associated with pain itself. Regarding the definition of chronic pain, The Institute of Medicine report on Relieving Pain in America states:

> *Chronic pain, by contrast, lasts more than several months (variously defined as 3 to 6 months, but certainly longer than "normal healing")…*[2]

We are focusing our investigation on chronic pain from the standpoint that chronic pain can be thought of as an illness itself. The Institute of Medicine states: "Chronic pain has a distinct pathology…it has significant psychological and cognitive correlates and can constitute a serious, separate disease entity."[2]. As with other diseases, it is imperative to understand the clinical features, morbidity, and disability associated with chronic pain.

Aside from duration, there are other characteristics that define a pathological pain state. Table 2.1 shows a list of these factors used in pain assessment. It is the consequences of pain that we are most interested in, to use the terminology here.

Table 2.1. Qualities of pain that are frequently measured in chronic pain populations

Pain symptoms	Definition	Measurement Instrument Examples
Intensity (or magnitude)	Strength of the painful sensation	Pain rating scales, visual analog scales (VAS)
Pain site	Where the pain is felt	Body diagrams, specific anatomical descriptions
Time of reference	When the pain was experienced	Prevalence measures such as current pain to past 3 months to pain ever
Consequences	How pain impacts an individual's activities	Disability indexes, Short Form-36 (SF-36), daily diary measures
Frequency	How often pain episodes occur	Number of episodes in a year
Duration	Length of pain since onset	0-6 months, 7 months to 2 years, 3 years or more
Source	Suspected cause of the pain	Typically, self-reported, frequently defined in exclusionary criteria such as "pain not due to fever or menstruation"

The term severity has been used as a synonym for intensity while others have used severity as a description of disability. Therefore, I have omitted it from the list of pain symptoms.

Using the biopsychosocial framework to describe pain as impacting the individual as well as their role in society, the US National Pain Strategy (NPS) has defined 'high impact chronic pain' as "persistent pain with substantial restriction of participation in work, social, and self-care activities for six months or more"[3]. This definition is similar to the time-frame of chronic pain (6 months) of focuses the definition of pain on the impact of the pain. Similar recommendations were made in 2014 by the NIH Task Force of Research Standards for Chronic Low Back Pain[4], acknowledging the failure to identify causes of pain and instead advocating a shift in focus to improving quality of life among people with pain.

Temporomandibular Disorder

Painful temporomandibular disorder (TMD) is a chronic condition characterized by pain in the jaw joint, face, and masticatory muscles. Although the definition of TMD depends on pain

around the temporomandibular joint, research suggests that TMD is a condition that also involves pain in many areas of the body[5]. The Surgeon General's Report "Oral Health in America" declared:

> *"Oral-facial pain… as a condition in and of itself, is a major source of diminished quality of life. TMD is considered an idiopathic pain disorder, along with several other chronic pain conditions of unknown origin, such as fibromyalgia, that are characterized by abnormal motor function, autonomic balance, sleep disruption, and neuroendocrine irregularities[6].*

This quote supports the conclusion above that chronic pain and specifically chronic orofacial pain should be considered as a potential source of decreased quality of life with serious characteristics listed above that contribute to an illness that goes beyond jaw pain.

The prevalence of TMD-like pain is measured by the National Health and Interview Survey (NHIS) and estimated at 6%[7] in 1989 and 4.6% in data pooled from 2000-2005[8]. Research addressing the prevalence of other pain and the systemic nature of impairment among people with painful-TMD supports the conclusion that while TMD is defined by joint pain, the personal experience of this condition likely involves comorbid pain conditions that compound impairment. For example, data from 2000-2005 NHIS found that less than 1% of those studied reported TMD-like pain without any comorbid headache/migraine, neck, or lower back pain and nearly 59% of people with TMD-like pain reported two or more of the following: headache, neck, back, and joint pain when asked about severe migraine/headaches, neck, back, and joint pain[8].

Disability

The task of defining and measuring health-related disability has a long history in medicine, psychology, sociology, and other disciplines. There is extensive literature exploring the meaning of disability, which delves into the concept from perspectives of economic, legal,

and social implications. Instead, I will explore the concept of disability that is assigned to oneself by a person with pain. The definition of disability developed by Nagi[9] and published in 1965 seems an enduring and succinct model for capturing the dimensions of disability applicable to people with chronic pain. Nagi defines disability as an individual's ability to fulfill "socially defined roles and tasks within the environment" within the framework shown below in figure 2.1. The Nagi model distinguishes disability from functional limitation, pathology, and impairment while acknowledging the relationships between the concepts with the use of double-sided arrows.

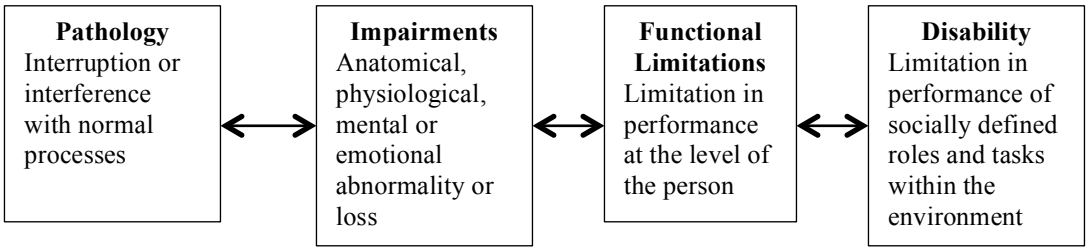

Figure 2.1. Nagi model of disability. Recreated from Nagi, 1965

Other conceptual models of disability

The World Health Organization (WHO) first published the International Classification of Impairments, Disabilities, and Handicaps (ICIDH) in 1980, presenting a framework for classifying the consequences of disease. As the Nagi model above, the ICIDH model (shown in figure 2.2) does not include pain as a factor in the depiction of disability.

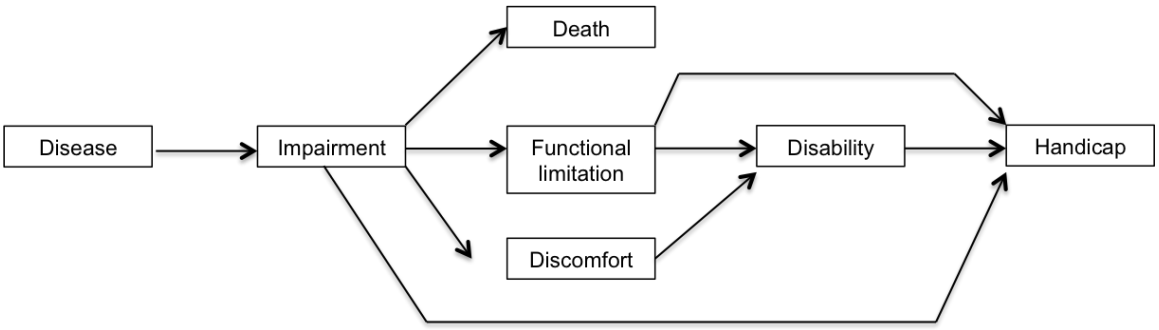

Figure 2.2. World Health Organization 1980 conceptural model of disease impact

The definitions of the key concepts in the model are shown in table 2.2 and are similar to Nagi's conceptual definitions. In contrast to Nagi's model, the ICIDH model contains only single-headed arrows, indicating impairment leads to functional limitation that leads to disability. The Nagi model has a more dynamic approach, recognizing that pathology, impairments, limitations, and disability can influence one another in bidirectional relationships and also indicating there is not a linear process from one variable to the next.

Table 2.2. Definitions of concepts used in WHO and Locker models
(adapted from Locker 1992[10] and WHO[11])

Concept	**Definition**
Impairment	
1988	Anatomical loss, structural abnormality or disturbance in biochemical or physiological proceesses which arises as a result of disease or injury or is present at birth
2001	Problems in body function or structure such as a significant deviation or loss
Functional limitation	
1988	Restrictions in the functions customarily expected of the body or its component organs or systems
2001	Functioning refers to all body functions, activities and participation
Disability	
1988	Any limitation in or lack of ability to perform the activities of daily living
2001	An umbrella term for impairments, activity limitations and participation restrictions
Handicap	
1988	The disadvantage and deprivation experienced by people with impairments, functional limiations, pain and discomfort or disabilities because they cannot or do not conform to the expectations of the groups to which they belong
2001	n/a

Locker[12] adapted the ICIDH model (figure 2.3), eliminated the starting point of disease, thus emphasizing the impact of intervening variables, and included new pathways. In this model, we see pain leading to disability and recognition of intervening variables that can influence impairment, limitation, and disability. While Locker's addition of pain to the model of the impact of health is helpful, the model is still restricted to single-headed arrows (other than intervening variables) and lacks arrows from limitation to pain and the impact of pain on limitation and impairment.

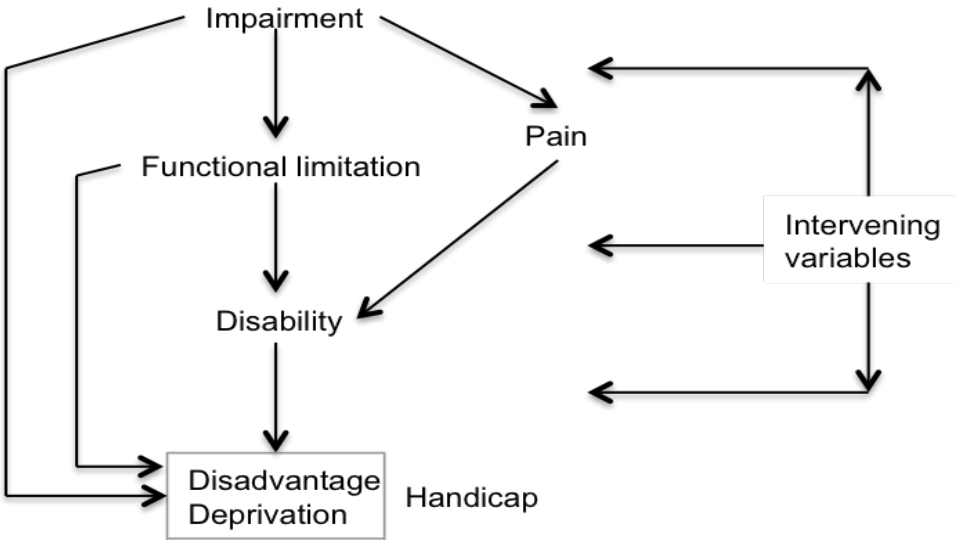

Figure 2.3 Locker's adapted International Classification of Impairments, Disabilities, and Handicaps (ICIDH) model

In 2001, WHO published the International Classification of Functioning, Disability and Health (ICF)—replacing the ICIDH as the "framework for measuring health and disability at both individual and population levels" (http://www.who.int/classifications/icf/en/)[11]. In this publication, the ICF eliminated the term 'handicap' and made broad changes to incorporate the

biopsychosocial framework of health as opposed to the medical or social models that did not take into account the interplay between health and social roles. Figure 2.4 shows the revised model published by the WHO in 2001. This model contains double-headed arrows denoting the complex relationships between the consequences of disease (impairments, limitations, and restrictions) but also a double-headed arrow indicating that health conditions can be influenced by limitations. This model represents a substantial improvement on previous models and comes the closest to the original Nagi model in terms of related concepts. In my opinion, the conceptual diagrams do not require a separate construct representing pain, particularly since pain can be defined as an impairment, a disease in itself, and/or a factor that influences limitations and restrictions we consider pain caused by another condition.

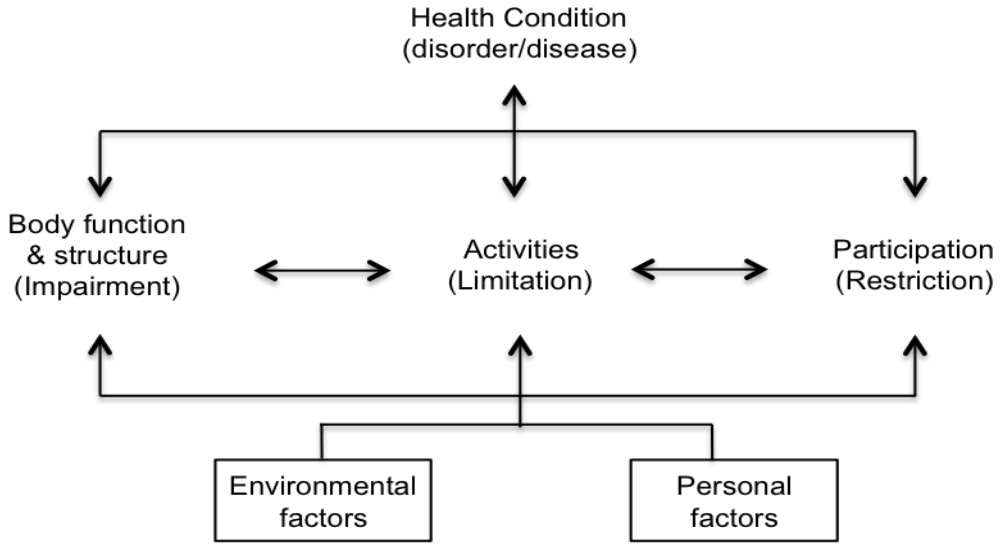

Figure 2.4. World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) 2001 model.

Disability and TMD

Disability associated with TMD has been studied using a variety of constructs: oral health quality of life (OHQoL), interference, functional limitation, and activities of daily living. We selected the most widely used measure of pain-related disability that is well validated and reliable: the Graded Chronic Pain Scale (GCPS). Two factors influenced the decision to use this measure: the generalizability and use of this scale in chronic pain populations other than TMD and the National Pain Strategy's recommendation for use of a chronic pain screening that assesses chronic pain severity and interference[13].

The GCPS was developed to measure the extent to which pain is perceived by the patient and the degree to which the pain is disabling[14]. The GCPS consists of 3 domains: characteristic pain intensity, interference, and disability days. Characteristic pain intensity (CPI) includes the average, current, and worst pain rated using a 0-10 Visual Analogue Scale (VAS). The interference scale asks about interference rated from 0 to 10 where 0 represents 'no interference' and 10 represents 'unable to carry on any activities'. Participants are asked to rate interference in three areas of life: 1) daily activities, 2) social, family, recreation, and 3) work activities. Disability days are calculated from a question asking how many days pain prevented participation in daily activities. These three domains and their subscales are combined to classify the chronic pain grade from grade 0 (representing no pain) to grade IV (representing high disability and high pain intensity)[15].

Review of literature

I performed a systematic review to explore what is known about the relationship between TMD and disability. See appendix A for MESH terms and search strategy. Briefly, a Pubmed search using search terms related to TMD resulted in 4,121 articles. Searches of CINAHL, Web

of Science, and PsyInfo yielded an addition 167 articles that were not duplicates listed in Pubmed. Initial filters were used to limit publications to English, research using human subjects, research enrolling adults 18 years and older, and elimination of duplicates resulted in 2,650 articles. All articles measuring pain-related disability and/or OHQoL, as an outcome of TMD or orofacial pain were included, requiring review of title titles among the restricted sample of 342 articles. Next, I reviewed 217 abstracts with the same criteria and further refined the number of articles to 178. Review of the 178 articles excluded all review articles, qualitative research reports, case studies, commentary, instrument development and validity studies. This left 56 articles that met the following criteria: human studies which included both TMD classification and either pain related-disability or interference assessment. Any study that measured only disability related to the jaw and not pain-related disability or a quality of life measure was excluded to capture studies concerned with overall disability and not limitations in the jaw area only. This limitation lead to a total of 35 studies for review.

Overwhelmingly, the Research Diagnostic Criteria (RDC) was the preferred method for assessing the presence of TMD. One study used the Oral Health Impact Profile (OHIP) and the GCPS[16] and reported that among both male and female participants, OHIP scores were higher among subjects with higher GCPS scores indicating oral health quality of life was lower among people with higher levels of pain-related disability. Another study used both the GCPS and the SF-12[17] in a longitudinal examination with follow-up 6 months after enrollment. The authors reported lower quality of life scores on the SF-12 were associated with higher chronic pain grades and pain intensity measured with the GCPS was the only significant predictor of GCPS pain-related disability at 6-months.

Among the articles, the major limitations of research are the use of convenience samples recruited from orofacial pain clinics or other specialty care facilities and a lack of consistent definitions of disability. The literature is reviewed in the next section.

Case control studies

The case control studies reviewed can be categorized by the comparison group: TMD compared to healthy controls[16, 18, 19] and people with TMD compared to people with chronic pain other than TMD, such as headache[20], neuropathic pain facial pain[21], and other chronic pain patients[22]. Among the three studies comparing people with TMD to healthy controls, all found TMD patients had significantly impaired functioning compared to healthy controls. All studies enrolled TMD patients from specialty or dental clinics except one that recruited a biracial (Caucasian and African American) sample of 830 women between the ages 19-23 who were screened for facial pain using the GCPS and then examined using the RDC examination for verification of TMD status. The authors report among 85 clinically confirmed cases, 74% had no or low pain disability (GCPS scores of 0 or 1) with no racial differences[18]. This is one of two articles reporting GCPS grades among TMD cases compared with controls[18, 19] (See table 2.3 for the distribution of GCPS among the samples). McKinney and colleagues[22] found TMD-only cases had less impairment of activity compared to the non-TMD chronic pain patients and overall the researchers concluded chronic TMD patients were behaviorally and psychologically similar to non-TMD chronic pain patients. These findings were based on the Chronic Pain Battery (CPB), a "multidimensional tool that collects essential medical, psychological, behavioral, social, and pain data", administered to 78 TMD cases compared with 98 non-TMD chronic pain patients. This finding supports the earlier assertion that pain functions

as a disease itself regardless of the anatomical site affected, and that the sequelae are not unique to the clinical classification of TMD chronic pain.

Cross-sectional studies

Among 14 cross-sectional studies reviewed, the majority used RDC criteria for TMD diagnosis with the exception of large population based surveys that relied on self-reported symptoms[23]. The majority of the studies used the GCPS to measure disability while one study used the MPI[24], and one study used the SF-36 to measure quality of life[25]. Again we see that when the OHIP and GCPS are used, there is a strong association between GCPS and mean OHIP scores.

One study enrolled potential community cases: a study of 183 dental students in Brazil who were surveyed for orofacial pain symptoms[26]. It is important to note that neither one of these studies, nor any other cross-sectional studies, enrolled self-identified TMD cases from the community. All studies reported that quality of life measures decreased as pain disability increased but also included small numbers of participants who reported pain-related disability.

Several studies reported low disability among study participants including one study of 111 patients recruited from a TMD and orofacial pain clinic summarized as: “GCPS scores showed that the vast majority of patients had a low disability or no disability at all, with only 5.4% of patients showing a severely limiting high disability”[27]. Four cross-sectional studies[28, 29] [30, 31] and two case control studies[18] [19] reported the distribution of GCPS grade among TMD patients. A summary of the distribution of GCPS is shown in table 2.3.

Table 2.3. Six research studies reporting GCPS scores by grade

Grade	**0**	**I**	**II**	**III**	**IV**	**Total**
Citation	%	%	%	%	%	N
Al-Harthy M, et al. (2010) [28]*	0%	45%	52%	2%	0%	46
Cioffi I, et al. (2014) [31]	7%	30%	35%	20%	6%	676
Licini F, et al. (2009) [29]	13%	27%	35%	14%	8%	308
Plesh O, et al. (2005) [18]	13%	60%	21%	4%	0%	61
Reissmann, D., et al. (2012) [19]	7%	34%	42%	10%	5%	70
Xu W, et al. (2011) [30]	22%	51%	18%	8%	0%	162

* Note: calculated based on percentages reported in paper

In 2015, Kotiranta[32] reported GCPS-related disability findings among 399 primary care patients seeking treatment for TMD. The GCPS was used to classify patients into one of 3 groups: 61% of the patients were classified as no-disability (GCPS score of 0), 27% to the low-disability (GCPS I and II) and 12% to the high-disability group (GCPS III and IV). The findings supported the use of the GCPS to classify patients with unique psychosocial subtypes and concluded the following:

> *"…patients in the high-disability group were those reporting the highest levels of symptoms of depression and somatization, sleep dysfunction, pain-related worry, and catastrophizing/ruminative thoughts. The low-disability group formed an intermediate group between those patients belonging to the no-disability group and those in the high-disability group across most variables studied."[32]*

This is important because this finding represents a dose-response relationship in categories of disability. Additionally, this finding supports other research reports that disability is associated with poorer overall functioning. If longitudinal research supports the conclusion that disability precedes depression, catastrophizing, and sleep disruption, then pain-related disability might be a vital indicator to predict quality of life.

One other study compared people with low to high-disability among 104 patients with TMD. RDC criteria were used to confirm TMD status and the GCPS was used to classify

patients as low (Grades I or II) or high-disability (Grades III or IV). The authors report patients with high levels of pain-related disability had significantly higher depression and somatization than those with low levels of pain-related disability[33].

Multiple studies found an association between pain-related disability, somatization and depression[33-37]. Catastrophizing was associated with disability measured using both the GCPS[38] and the MPI[24].

Longitudinal studies

Eleven longitudinal studies met the criteria for review: 1) enrolled TMD patients and 2) measured disability. Six studies used the GCPS to measure disability, two used the MPI, one study used both the GCPS and the SF-12[17], one study used the GCPS and the SF-36[39], and one study used the CGPS and MPI[40].

Two studies published by Epker (1999 [41] and 2000 [42]) used similar samples of TMD patients referred to research by dentists and oral surgeons. The outcome for each study was chronicity of TMD measured with follow-up at 6-months after enrollment. Although the studies used RDC verification of TMD status at enrollment, the follow-up appointments at 3 and 6-months were conducted over the phone, thus introducing potential bias. Researchers were able to conclude that the characteristic pain inventory items from the GCPS accurately classified 91% of the 144 subjects who went on to develop chronic TMD at follow-up[41] and that the MPI interference score at baseline accurately predicted treatment-seeking behavior in 76% of the sample of 177 acute TMD patients[42].

In a 6-month study of 152 RDC verified TMD patients from a specialty clinic in Sweden, Galli[17] found GCPS score at baseline was the only significant predictor of GCPS score at follow-up. Pain-related disability could be predicted at the 3-month follow-up by depression and

anxiety scales, but this trend did not hold for the 6-month follow-up. Unfortunately, the follow-up in this study was performed using self-reported questionnaires via mailing instead of a clinic appointment with a repeated RDC examination.

Velly and colleagues (2011) [43] conducted an 18-month prospective study of TMD among 480 people with the aim of evaluating the effects of catastrophizing and depression on progression of pain-related disability using the GCPS. They found disability score at follow-up was related to baseline catastrophizing, depression, widespread pain, and GCPS at baseline. No significant association was noted with gender or age. In adjusted analysis including all variables, baseline catastrophizing, depression, and GCPS at baseline remained positively related to disability score at the 18-month follow-up. A small association was observed between widespread pain and disability. A strength of this study is the community-based sample however the sample did not have a large group of participants with high level disability, only 12% of the population (n=70) at baseline and only 54 people at follow-up met disability criteria. Data from the same sample was published one year earlier with the focus of investigation on the effect of fibromyalgia and widespread pain on TMD. In their article, the authors report "Baseline widespread pain (OR: 2.53, P = .04) and depression (OR: 5.30, P = .005) were associated with onset of clinically significant pain (GCPS II-IV) within 18 months after baseline"[44].

In 1998, Garofalo published a paper exploring the transition from acute to chronic TMD among 153 TMD patients, 87 of which met criteria for chronic TMD at 6-month follow-up. GCPS score of III or IV was a predictor of chronicity (patients with higher GCPS scores were more likely to be in the chronic group at follow-up) along with an interaction between sex and muscle pain (as opposed to disc displacement or other types of joint conditions)[15].

Phillips and colleagues addressed the effect of gender on 6-month follow-up of acute to

chronic TMD status among 233 patients. The authors reported women who developed chronic TMD had higher mean scores on the interference score of the MPI but found no significant difference among men[40].

John[45] focused on the association of widespread body pain among 397 patients with TMD as a potential risk factor for dysfunctional TMD (which they defined as GCPS score of II with any disability points, III, or IV) by performing interviews at enrollment and follow-up at 1 and 2 years. After controlling for age, education, depression, and baseline GCPS, the authors found widespread pain was a risk factor for dysfunctional TMD (OR=1.9). Widespread pain was defined as self-reported pain in response to the question: *In the last 6 months, have you had a problem with back ache or back pain (chest pain, stomach ache or pain, severe headache or migraine)?*[45].

Reisine studied the quality of life among 30 TMD patients at their first treatment visit and follow-up at 1-month and 6-months after first treatment visit. The MPI was used to assess pain interference which was reported to improve 6-months after enrollment[46].

One study[47] found that 50% of 100 patients improved after 6 months with duration of pain being the strongest predictor or lack of improvement. The authors emphasized that no psychosocial factors predicted improvement although a number of variables of interest including age, gender, anxiety, catastrophizing, and psychological distress were assessed. The authors also collected data on widespread pain and jaw limitation and found these variables to not be predictive of improvement. Duration of pain, number of healthcare providers seen and reported hindrance on function all predicted 6-month improvement[47]. Functional limitation (measured using the 'Patient Specific Approach' assessed hindrance of function on a 0-100 VAS score) but not disability at baseline predicted improvement at 6-months. However, it is important to note

that the follow-up measurement was a questionnaire asking the patients if their pain had disappeared, decreased, remained the same, or increased.

Randomized controlled trials

Six RCTs met the criteria for review: 1) enrollment of people with TMD and 2) measurement of disability[48-53]. RCTs were not restricted by intervention and included studies of cognitive behavioral treatment (CBT) interventions, biofeedback, and stress reduction training. Among these studies, three used the GCPS to measure disability[48, 51, 52, 54], two used the MPI[49, 50] and one study used an interference with daily activities questionnaire with a 0 to 10 scale[53].

Rudy and colleagues[50] enrolled 133 patients from a TMD clinic in a 6-week treatment with interocclusal appliance therapy as well as 6-week biofeedback relaxation and stress reduction treatment. Participants were examined prior to treatment, post-treatment, and 6-months after completion of treatment. The researchers measured disability using the MPI interference score and found overall the treatment program was associated with decreased interference when pre-treatment and 6-month follow-up were compared. Additionally, the researchers used the MPI to categorize patients into one of three groups: dysfunctional, interpersonally distressed, and adaptive copers. The dysfunctional group was characterized by psychological distress and high levels of pain-related interference. This dysfunctional group demonstrated the most improvement from therapy compared to the other two groups. This finding suggests patients fitting the dysfunctional profile assessed by the MPI would benefit the most from standard therapy with biofeedback and stress reduction treatment.

Turner[53] enrolled 139 TMD patients (classified by self-reported facial ache or pain in the temporomandibular joint) from an HMO or specialty clinics to participate in a study

comparing standard treatment to standard treatment with cognitive behavioral therapy. Disability (defined as interference due to pain on a 0 to 10 scale), depression, pain, coping strategies, and jaw opening were measures pretreatment and at 3- and 12-month follow-up. The authors reported that at 3-month follow-up, demographic variables, treatment group, and belief/coping measures did not predict pain interference with activities when pre-treatment pain interference was controlled for statistically. This finding indicates pain interference at follow-up may have been linked to a variable not measured.

Three studies limited enrollment to patients with a GCPS score of 2 or higher (Dworkin 2002 [48], Turner 2006 [52] and Turner 2007 [51]) recruited from specialty clinics. All three studies used the RDC to verify TMD patient status and the GCPS to measure disability. Dworkin[48] compared usual treatment (described as physiotherapy, patient education, medications, and occlusal appliance therapy) with usual treatment plus a 6-session cognitive behavioral intervention and measured variables at baseline, post-treatment follow-up at 6- and 12-months. The authors reported the CBT intervention was effective in improving pain-related interference. They also reported depression severity measured at baseline was associated with pain interference at baseline, but not as much with interference at one-year follow-up.

In 2006, Turner[52] reported results from a study of 156 TMD patients randomized to CBT or a control patient education group and found “the proportion of patients who reported no interference at 12 months was nearly three times higher in the CBT group than in the control group”. In a publication one year later, Turner[51] reported pain-related beliefs mediated CBT effects on disability at one-year follow-up among 115 TMD patients.

A single RCT enrolled people with RDC verified TMD from the community. In this study, 101 people were recruited with community advertisements and randomized to standard

treatment or standard treatment plus CBT and were assessed at post-treatment (6 weeks), 12, 24, 36, and 52-weeks. The main finding indicated somatization moderated the effect of treatment on pain-related interference measured by the MPI[49]. This finding supports the conclusion that somatization is involved predicting pain-related disability.

Conclusions

In summary, this literature review has identified four themes that warrant further investigation and that have motivated the aims and methods planned for this study: 1) disability has been associated with the following characteristics: depression, somatization, catastrophizing, and anxiety, 2) there is a paucity of research involving community based TMD cases, 3) few studies have focused on pain-related disability in a sample that is diverse and can be stratified by gender, race, and other identified variables, and 4) no studies have reported disability results in conjunction with clinical findings other than jaw limitation.

The aims of this dissertation were intended to address identified gaps in the research by using established and validated scales to measure pain-related disability among community dwelling cases. The variables included in analysis allowed for conclusions about pain sensitivity, clinical features of pain in the face as well as in the body in addition to exploring the role of variables that have been identified in previous research. This choice allows for a validation of previous findings while also considering variables that have not been previously explored—specifically experimental pain sensitivity. The large sample size permits multiple comparisons and examination of the role of multiple sociodemographic characteristics that may not have been present in the majority of the reviewed literature. Finally, we seek to explore the relationships between these factors as measured using latent variables that can contribute to the understanding of complex relationships.

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CHAPTER THREE: RESEARCH DESIGN AND METHODS

Study Population

Men and women ages 18-44 were recruited into the parent study from four sites: NC, NY, FL, and MD. The four study sites are all centered in east coast college towns but represent rural and urban populations with varying demographics. The source population was the counties surrounding the study sites. Table 3.1 shows demographic characteristics of the study sample. Individuals with major medical conditions such as kidney disease, heart disease, chronic respiratory disease, uncontrolled hypertension, epilepsy and/or uncontrolled diabetes were excluded. Also, hospitalization for psychiatric treatment within the previous 6 months was exclusionary. The gender and ethnicity enrollment was designed to reflect demographic characteristics in the major counties surrounding the four study sites.

Prospective participants responded to recruiting materials seeking volunteers with jaw pain while healthy controls were recruited for a "study of muscle and jaw function" and had no history of jaw pain. It is possible that the sample is not representative of orofacial pain in the community, particularly if people who volunteer for research studies are fundamentally different than those who would not be willing to participate in a research study. The importance of studying a community-based sample as opposed to recruiting specifically from orofacial pain clinics and dental clinics allows for greater generalization to the community dwelling people with chronic TMD. This is a problem faced by most research studies and the OPPERA study is not immune to the potential bias introduced when random sampling cannot answer the research

question. However, the relatively large sample size should provide results that are generalizable to people with TMD.

Although duration of pain was not associated with disability in preliminary analysis, people with onset TMD may have had less time to develop coping strategies, less experience with treatment seeking, and other factors that may distinguish them and provide insight into the onset period where intervention might be most effective.

Table 3.1. Demographic variables describing the data from the OPPERA study of 1088 chronic TMD cases.

Characteristic	N	Column %
Gender		
Male	253	23.3
Female	835	76.7
Age (years)		
18-24	385	35.4
25-34	395	36.3
35-44	308	28.3
Race/Ethnicity		
White	765	70.3
Black or African American	175	16.1
Asian	45	4.1
Hispanic	66	6.1
Other/not stated	37	3.4
Study Site		
Chapel Hill, NC	342	31.4
Buffalo, NY	247	22.7
Gainesville, FL	271	24.9
Baltimore, MD	228	21.0

Study Design

I addressed the stated aims using chronic TMD cases recruited as part of the case control design of the Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) study. Aims 1 and 2 utilized data from the cross-sectional study of 1088 people with chronic examiner verified TMD. The next section details each aim with the corresponding research question, rationale, and objectives before a discussion of the outcome variable and covariates of interest.

Aim 1: Explore associations between sociodemographic, psychological distress, clinical features, and experimental pain sensitivity domains and high-impact pain among people with chronic TMD

Research question

What characteristics are associated with high levels of disability?

Rationale

Understanding factors associated with high disability in a large cross-sectional study has implications for understanding disability longitudinally. Knowing more about characteristics that are common among people with high disability is useful for clinicians tailoring interventions to reduce disability and targeting modifiable factors that may influence disability level.

Objectives

We used binary logistic regression to discriminate between low and high pain-related disability groups. We undertook a model-building strategy that started with demographic variables and then built upon this model by adding variables addressing the domains of psychological distress, TMD clinical features, and experimental pain sensitivity. We evaluated the models using area under the curve values to determine the best discriminatory model.

Aim 2: Create and evaluate a structural equation model of pain-related disability in people with TMD with factors representing psychological distress, clinical TMD features, and experimental pain sensitivity

Research Question

What are the factors contributing to disability and what are the relationships among those factors?

Rationale

Identifying the factors associated with increased disability is vital for improving targeted interventions and reducing the burden of chronic TMD.

Objectives

The primary goal was to fit a model with latent variables measuring pain-related disability, psychological distress, experimental pain sensitivity, and clinical TMD features. First, I re-validated the GCPS with the inclusion of a variable measuring presenteeism. Second, I created measurement models for psychological distress, experimental pain sensitivity, and clinical TMD features based on self-report and clinically measured observed variables. Subsequently, I fit a full SEM with pain-related disability, psychological distress, experimental pain sensitivity, and clinical TMD features.

Outcome assessment: Pain-related disability

Graded Chronic Pain Scale

The Graded Chronic Pain Scale (GCPS) contains 7 items asking participants about pain intensity, interference in daily activities, and disability days (days with decreased or impaired functioning). These seven items are used to calculate a score from 0 to IV. Grade 0 indicates no pain, grade I is defined as pain of low intensity, grade II-low and grade II-high refer to high intensity pain with low grade II referring to no disability and high grade II indicates the presence of disability, grades III and IV represent moderate and significant pain-related disability (independent of pain intensity) respectively. A middle cut-point has been recommended to distinguish between low and high levels of disability using the GCPS[1]. This cut-point replaces previous recommended use of grades I and II to denote low and grades III and IV as described in the literature review above. This cut-point has been used in research since 2002 to distinguish

between low and high-disability as well as functional and dysfunctional status[1]. The GCPS has an established cut-point that is widely accepted and used in clinical research[2].

Previous research reported the prevalence of pain-related disability among people with TMD measured with the GCPS range from 2%[3] to 41%[4]. The expected prevalence of disability using the GCPS cut-point in this sample was 35% based on preliminary analysis. The GCPS has been used to evaluate pain-related disability in a number of research studies including studies of TMD[5, 6] and has been reported to be a reliable and valid instrument[7, 8]. We used the dichotomous cut-point of low vs. high to address aim one and created a continuous latent variable of pain-related disability based on all components of the GCPS in the analysis used for aim two.

Covariate assessment

Covariates included a mix of self-reported and clinical measurements variables representing the following domains: sociodemographic, clinical TMD features, psychological distress, and experimental pain sensitivity. Each measure is shown in table 3.2 with a description of the measured variable and the coding scheme.

Table 3.2. Variables with description and coding

Variable	Variable description	Type of variable	Coding
Sociodemographic domain			
Age	Self-reported in years	Continuous	18-44
Gender	Self-reported at enrollment	Binary	0 = male 1 = female
Race/Ethnicity	Self-reported at enrollment	Nominal categorical	0 = White non-Hispanic 1 = African American 2 = Hispanic 3 = Asian 4 = Other including multi-racial
Study site	Assigned based on initial interview for eligibility for study	Nominal categorical	0 = UNC 1 = UB 2 = UMD 3 = UFL
Psychological distress			
Positive affect	Profile of Mood States (POMS-Bi) Positive Affect summary score	Continuous	30-120
Negative affect	POMS-Bi Negative Affect summary score	Continuous	30-120
Somatic symptoms	SCL-90R Somatization scale	Continuous	0-4
Catastrophizing	Coping Strategies Questionnaire (CSQ-R) catastrophizing subscale	Continuous	0-6
Clinical TMD features			
Jaw opening	Maximum unassisted opening measured in millimeters	Continuous	0-70mm
Jaw limitation	Jaw Functional Limitation Scale (JFLS) Global measure scale	Continuous	0-10
Oral parafunctions	Oral Behavior Checklist (OBC)	Continuous	0-84
Pain duration	Years since pain onset	Continuous	0-99
Number of painful body sites	Number of body sites reported as painful upon examination	Continuous	0-14
Number of comorbid conditions	CPSQ count of presence of 20 self-reported comorbid conditions	Continuous count	0-20
Experimental pain sensitivity			
Thermal tolerance	Thermal pain threshold and tolerance	Continuous	32-52° C
Pressure pain threshold	Pressure pain threshold (trapezius) kPa	Continuous	50-600 kpa
Mechanical pain rating	Pain rating of mechanical flat-tipped probe	Continuous	0-100
Mechanical pain temporal summation	Difference in pain rating from single stimulus to series of ten	Continuous	-13.7-80

kPa=kilopascals

Statistical Methods

Statistical analysis applied conventional epidemiologic methods to address the stated aims with the primary outcome measure of disability as defined using the GCPS. Both aims were limited to a sample of prevalent chronic TMD cases. Aim 1 evaluated factors are associated with prevalence of high pain-related disability among people with chronic TMD. Aim 2 evaluated a model of pain-related disability using structural equation modeling.

Among continuous variables we explored the distribution of the variable among people with high and low disability and performed t-tests to compare mean scores by disability status. Additional univariate statistics were generated with stratified contingency tables. In the case of binary and categorical variables, I used a defined a reference value. Among continuous variables, I explored the distribution to determine appropriate cut-points. However, since there are not previously defined cut-points for the continuous variables, I used tertiles in order to make comparisons based on low, medium, and high groups.

Missing data was evaluated for each variable and compared by tertile and outcome (low disability vs. high disability). Participants who completed less than half of the items in a questionnaire were not included in analysis. In the group with at least 50% completion, multiple imputation was performed using the expectation maximum method before I obtained the datasets. As a sensitivity analysis, I performed a complete case analysis restricted to participants with complete data for all variables included in the full regression model (n=846) and then compared results to a more complete sample (n=1014) of participants with complete data for all variables in the selected model. Secondly, I compared both results to data after performing multiple imputation. Discrepancies were evaluated. The extent of missing data between people with low and high disability was examined.

Statistical power

Aim 1 addressed factors useful in discriminating between people with low or high pain-related disability. Aim 2 explored factors contributing to the latent variable of pain-related disability. Aim 1 involved hypothesis testing assuming a background disability prevalence of 20%. Given the study sample size of 1,046 with complete data for the outcome of interest, this study would have 80% statistical power for detecting differences in prevalence ratios comparing low and high disability above the level of 1.4 and greater. See Figure 3.1. For example, in a reference population with prevalence of 0.30, a prevalence ratio of 1.6 has 80% power.

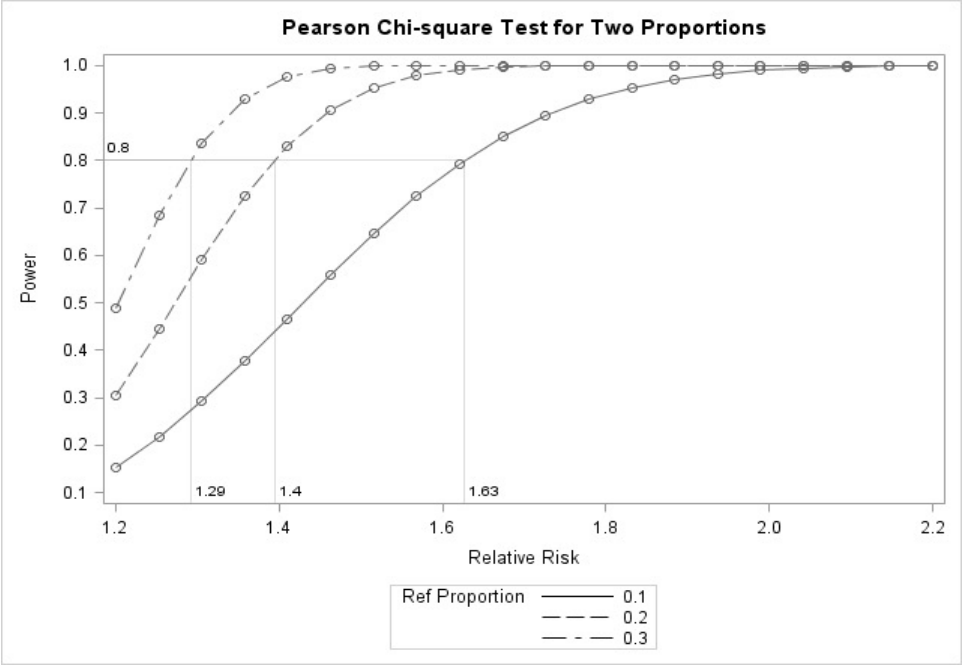

Figure 3.1. Statistical power curves for aim 1 calculated using SAS 9.3

The SEM for aim 2 was adequately powered given the ratio of sample size to number of parameters to be included in the model. Using a calculator for sample size, I tested several parameters and found that with a desired statistical power level of 0.80 and an anticipated effect size of 0.3, a SEM with 7 latent variables and 20 observed variables with a probability level of

0.05 requires a minimum sample size of n=170 to detect effect and a recommended sample size for model structure of n=223 (http://www.danielsoper.com/statcalc/calculator.aspx).

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CHAPTER FOUR: CHARACTERISTICS ASSOCIATED WITH HIGH-IMPACT PAIN IN PEOPLE WITH TMD: A CROSS-SECTIONAL STUDY[1]

Overview

Background: High-impact (disabling) pain diminishes quality of life and increases health care costs. This study aims to evaluate the characteristics that distinguish between high and low-impact pain among individuals with painful temporomandibular disorder (TMD).

Methods: Community dwelling adults (n=846) with chronic TMD completed standardized questionnaires assessing four domains: 1) sociodemographic, 2) psychological distress, 3) clinical pain, and 4) experimental pain. We used high-impact pain, classified using the Graded Chronic Pain Scale, as the dependent variable in logistic regression modeling to evaluate contributions of variables from each domain. Cross-validated area under the ROC curve (AUC) quantified model discrimination.

Results: One third of participants had high-impact pain. Sociodemographic variables weakly discriminated between low and high-impact pain (AUC=0.61, 95% CI 0.57, 0.65) with the exception of race. An 18-variable model encompassing all four domains had good discrimination (AUC=0.79, 95% CI 0.75, 0.82), as did a simplified model (sociodemographic variables plus catastrophizing, jaw limitation, and number of painful body sites): AUC=0.79, 95% CI 0.76, 0.82). Duration of pain, gender, and experimental pain testing results were not predictive.

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Conclusion: High-impact chronic pain is a common problem among people with painful TMD. Assessment of characteristics associated with high-impact pain can be easily performed to identify modifiable risk factors and reduce high-impact pain.

1 Introduction

TMD is a public health problem

Temporomandibular disorder (TMD) is characterized by pain in the jaw joint, face, and masticatory muscles that can become chronic. Although the hallmarks of TMD, as a regional pain disorder, are pain in the temporomandibular joints and masticatory muscles, people with TMD often experience pain in many other areas of the body[1].

Population-level prevalence of TMD range from approximately 5-10%, though case definitions vary among studies. Based on a single-item question, The National Health and Interview Survey (NHIS) estimated TMD-like pain at 6% in 1989[2] and 4.6% in data pooled from 2000-2005[3]. A representative sample of an urban population in Brazil found 9.2% of people reported experiencing at least 3 TMD symptoms[4]. The prevalence of TMD combined with the paucity of effective treatments, and the likelihood of comorbid conditions such as headache and other idiopathic pain conditions, result in a significant individual and public health burden. For example, high-impact pain measured by Graded Chronic Pain Scale (GCPS) is predictive of healthcare spending. Specifically, among orofacial pain patients, movement from low to high GCPS status results in a $525[2] increase in healthcare costs over 6 months[5].

[2] The reference reported 2012 £366 which we converted to 2012 US dollars using http://eppi.ioe.ac.uk/costconversion/ (last accessed February 27, 2018).

High-impact pain

The National Pain Strategy identified as a target "Reducing the prevalence of high-impact chronic pain and its associated morbidity and disability"[6]. However, the extent of TMD-related disability is disputed. In a study of nursing students with signs or symptoms of TMD, 93.7% reported not having sought treatment, of whom nearly half (46%) reported that they were not bothered by the symptoms[7]. The authors inferred that the symptoms were not a problem for these individuals and concluded "most subjects with clinically detectable dysfunction are *functioning adequately* without significant symptoms" (p. 295) [emphasis added]. In one study of 399 TMD patients, only 49 (12%) met criteria for high-pain related disability[8]. Reported prevalence of pain-related disability classified using the established taxonomy of Graded Chronic Pain Scale (GCPS) among people with TMD range from 2%[9] to 41%[10]. Using the same outcome assessment to obtain vastly different prevalences warrants further investigation. In truth, the extent of the problem of high-impact pain among people with chronic TMD is unknown.

Research exploring pain-related disability among people with TMD has identified multiple potential characteristics associated with disability. Researchers have reported an association between pain-related disability, somatization and depression[11-15]. Catastrophizing has been associated with high pain-related disability[16, 17]. Pain intensity and disability points have been associated with anxiety, somatization and depression[18]. Along with depression and somatization, duration of pain was linked to pain-related disability in Dutch, Italian, and Israeli samples[19]. Limitations of previous observational studies include potential selection bias from recruitment of participants from specialty pain clinics as some other factor may influence both treatment-seeking and pain-related disability. Many studies have reported a low number of

people experiencing high pain-related disability. Small sample size has prevented thorough examination of multiple factors in the respective population.

The purpose of this study was to identify variables from four domains that are associated with high-impact pain.

2 Methods

Study overview

This cross-sectional study comprised 1088 people with chronic TMD recruited between May 2006 and October 2013 addresses characteristics associated with high-impact pain. The sample was nested in the parent study, the Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA; Slade et al 2011[20]). The parent OPPERA study included a case-control study that compared chronic TMD cases with TMD-free controls. Human Research Ethics Committees at all study sites approved the study protocol. All participants signed an informed consent for study participation. Participants were compensated for their time.

Participants

Participants were community dwelling individuals living near one of four study sites (University at Buffalo, NY, University of Florida Gainesville, FL, University of Maryland in Baltimore, MD, and University of North Carolina at Chapel Hill, NC) of the OPPERA study. Participants responded to advertisements seeking people with chronic jaw pain. Participants were aged 18-44 years and were required to be fluent in English. Exclusion criteria included recent facial surgery or facial injury, pregnancy, orthodontic procedures or major medical conditions including kidney disease or uncontrolled hypertension. For more details about recruitment and sociodemographic composition of participants from each study site see Slade et al.[20].

Participants completed a telephone interview to assess eligibility prior to completing a battery of questionnaires about psychological distress and clinical pain, and a 3-hour clinic visit including clinical examination for verification of TMD status and experimental pain testing. Of the 1088 TMD cases recruited, 1042 had data for the outcome of interest and hence were included in the current study (see figure 4.1). See supplemental material for a diagram of participants contacted, eligible and consented.

Procedures

Chronic TMD was defined as self-reported facial pain symptoms experienced for at least 6 months prior to enrollment and fulfillment of examination criteria described below. The 6-month threshold is consistent with the definition of chronic pain provided by the Institute of Medicine: "Chronic pain, by contrast, lasts more than several months variously defined as 3 to 6 months, but certainly longer than 'normal healing'"[21]. Potential participants had to report pain in the cheeks, jaw muscles, and/or jaw joints for at least 15 days in the prior month and at least 5 days per month for the previous 5 months. The Research Diagnostic Criteria for TMD (RDC/TMD) is a structured clinical examination conducted by a calibrated investigator who obtained measurements of jaw movement, records joint sounds, and palpates muscle and joint sites to determine the classification of painful TMD or normal[22]. This examination was based on the established guidelines of the RDC/TMD[23].

Outcome assessment: Disability

We measured pain impact using dichotomized scoring from the Graded Chronic Pain Scale (GCPS). The GCPS contains 7 items to assess pain intensity, interference in daily activities, and disability days (number of days with decreased or impaired functioning). These seven items were

used to calculate five, hierarchical categories: grade 0 to grade IV[24]. Categories were subsequently dichotomized to denote low-impact (GCPS grades IIa-low or less) or high-impact (GCPS grades IIb-high or more) following the algorithm developed by Dworkin[25]. The GCPS has been used to evaluate pain-related disability in a number of research studies including studies of TMD[26, 27] and has been reported to be a reliable and valid instrument[24]. When the GCPS was published, the researchers used the term "pain-related disability" but recently the National Pain Strategy's Population Health Strategy for Pain report indicates that high-impact pain and pain-related disability refer to the same construct.

Explanatory variables

The multidimensionality of pain impact was assessed using variables from multiple domains. Sociodemographic data were collected upon entry (study site, age, self-reported sex and racial identity). Psychological distress variables measured positive and negative affect, catastrophizing, and somatic symptoms. Clinical pain features represent a mix of self-report measures related to jaw function such as jaw limitation and oral parafunction behaviors, and variables obtained during clinical examination. Experimental pain variables were collected during laboratory sensory testing. Although not previously explored in research addressing pain impact, experimental pain sensitivity has been linked to clinical pain expression[28]. Explanatory variables fit into four domains: sociodemographic, psychological distress, clinical pain, and experimental pain sensitivity. This categorization is consistent with domains of interest defined by OPPERA investigators[29].

Jaw mobility and painful body sites

Examiners measured two aspects of jaw function that were not part of the RDC/TMD criteria for case classification: 1) maximum unassisted opening and 2) number of painful body

sites. Instructions for the unassisted mouth opening measurement were "Open as wide as you can even if you feel pain or increase any pain you are feeling" and opening distance was measured in millimeters. To assess the number of painful body sites, pressure was applied to seven sites bilaterally including: the trapezius, supraspinatus, second rib, lateral epicondyle, medial gluteus, greater trochanter, and medial knee[23]. At each site, three pounds of pressure was applied. The respondent reported pain or no pain at each site for a sum score from 0-14.

Jaw limitation

The Jaw Functional Limitation Scale (JFLS) is a self-administered 20-item instrument that measures limitations in three areas: chewing limitation, vertical jaw mobility or opening limitation, and limitation in verbal and emotional expression[30]. Participants were asked to rate their limitation in activities such as "chew tough bread" and "open wide enough to bite into a sandwich" using a 0 to 10 scale where 0 represented no limitation and 10 indicated severe limitation. The JFLS can also be used to calculate a combined global measure of jaw limitation. We used the global functional limitation measure as an overall summary of jaw limitation.

Oral Parafunction/Jaw overuse behaviors

The Oral Behavior Checklist (OBC) is a 21-item instrument to assess the frequency of a variety of oral parafunctional behaviors such as grinding the teeth at night, chewing gum, and sustained talking[31]. The participants were asked to report how often they engage in these behaviors answering with ordinal responses from 0 to 4 indicating the frequency of the behavior. We used the summary score of all items.

Comorbid pain conditions

Participants completed a questionnaire that asked about the presence or absence of 20 conditions: joint disease or arthritis, fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, tendency to faint, ringing in ears, periodic heart racing or pounding, repeated trouble with neck, back, or spine, insomnia, depression, panic disorder, post-traumatic stress disorder, anxiety disorder, acid reflux, interstitial cystitis, prostatitis, multiple chemical sensitivity, dysmenorrhea, chronic pelvic pain, and sleep apnea. We used a sum score ranging from 0-20 corresponding to the number of conditions positively endorsed by participants.

Duration

Participants reported the time (in years and months) since facial pain began. Duration was intended to measure the time since initial onset of the condition and not the time elapsed during the most current pain episode. A separate question was asked of participants to describe the pattern of duration of pain using the following categories: persistent, recurrent, or a single episode that had since ended.

Psychological Distress

Positive and Negative affect

Participants completed the Profile of Mood States-Bipolar (POMS-Bi), a 72-item inventory used for assessing mood profiles. The scoring produces 6 dissimilar phases of mood that can be summed into two scores: overall positive affect and overall negative affect[32]. These scores capture the multiple domains assessed with the POMS-Bi including feelings of confidence, confusion, hostility, anxiety, and depression. We hypothesized the negative

summary score would encapsulate anxiety and depression that may be associated with high-impact pain.

Catastrophizing

Catastrophizing was classified according to the catastrophizing subscale of the Coping Strategies Questionnaire (CSQ-R). The CSQ-R is a revised version of the original CSQ[33] which consists of 27 items relating to how individuals cope with pain. Participants indicate the frequency with which they engage in specific coping activities when experiencing pain, using a 7-category numerical scale ranging from 0 (never do that) to 6 (always do that). The catastrophizing subscale is comprised of 6 questions indicating negative statements such as "I worry all the time about whether it will end". This subscore addresses the concept of pain-related worry previously reported to be associated with high levels of pain-related disability[8].

Somatic symptoms

Participants completed the Symptoms Checklist 90-Revised (SCL-90R), a 90-item self-report inventory of symptoms the participant may have experienced. Participants were instructed to answer how much each problem distressed or bothered them during the past 7 days with the following ordinal scale: not at all, a little bit, moderately, quite a bit, or extremely. These items were scored 0 to 4 accordingly. The SCL-90R includes a somatization subscale that consists of questions about headaches, chest pain, lower back pain, nausea, sore muscles, faintness, trouble getting your breath, hot or cold spells, numbness, a lump in the throat, feeling weak in parts of the body and feeling heaviness in arms or legs[34].

Experimental pain

Thermal tolerance

A commercially available thermal stimulator (Medoc, Israel) was placed on the participant's arm, producing temperature increasing at a steady rate of 0.5°C/second. Participants were asked to click a mouse button when they no longer wished to tolerate the pain from the heat and this temperature was recorded as the thermal tolerance. This procedure was repeated four times and the average was recorded as the participant's thermal tolerance.

Pressure pain threshold

Pressure pain thresholds were measured using a pressure algometer (Somedic, Sweden) placed on multiple body sites. The participants were given instructions to press a button when he/she first felt a sensation of pain from pressure. The rating is a single number, the average from two ratings on each side of the body reported in kilopascal units of pressure. For the analysis reported here, we used the pressure threshold measured on the trapezius. This site was selected to capture pain sensitivity outside the orofacial area. The trapezius site has been defined as a fibromyalgia tender point[35] and therefore may be a marker for widespread body pain.

Mechanical pain rating and mechanical temporal summation

Mechanical pain ratings and temporal summation of mechanical pain were assessed using a flat-tipped weighted pinprick stimuli applied to the skin. Participants were asked to rate the sensation from the weighted stimuli using the 0-100 pain intensity scale. Temporal summation of pricking pain was tested with the weighted mechanical probe applied in a series of ten applications over 10 seconds. Again, participants were asked to rate the pain intensity evoked by

the series of stimuli using the 0-100 scale. Temporal summation was calculated as the difference between the rating of the series-of-10 stimuli and the rating of the single stimulus.

Data analysis

The outcome of interest was dichotomous pain-related disability score, classified using the GCPS. Student's t-tests were used to compare the mean values of continuous variables between low and high disability groups. Correlations between pairs of continuous variables were computed using Spearman's rank correlation coefficient to identify variables that should be excluded from analysis due to potential for multi-collinearity. There were no variables with correlation higher than 0.7 thus none were excluded. For descriptive purposes, tertiles of continuous variables were used to establish low, medium, and high-levels because category cut-points have not been previously defined. Categorical variable classification was used for frequency and stratified analysis.

Binary logistic regression was used to evaluate associations between high-impact pain and the associated risk variables comprising sociodemographic, psychological distress, clinical pain, and experimental pain domains. Prevalence odds ratios from logistic regression were used to calculate area under the ROC curve (AUC) statistics in order to provide a simple numeric summary of a multivariable model's ability to discriminate between people with low- vs high-impact pain. To address the problem of overfitting when calculating AUC, we used a cross-validation method for estimating prediction error by creating divisions of the dataset for training and validation of the fitted model. The process involves simulation of model fitting without observations and then using that model-fit result to compute the result for the previously excluded observations[36]. Cross-validation is a more efficient substitute for the classic method

of splitting a dataset and using one section to create the predictive model and then testing the model in the other section.

The model building strategy started with a model including only sociodemographic variables (i.e. Model 1 in Table 4.4). Subsequent models explored the additional contributions of variables corresponding to the following domains: psychological distress (Model 2), clinical pain (Model 3), and experimental pain (Model 4). Model 2 included model 1 variables plus psychological distress variables: positive and negative affect scores, somatization subscale, and catastrophizing subscale. Model 3 included all variables from previous models with the addition of clinical pain variables: JFLS global score, OBC summary score, maximum unassisted opening, number of painful body sites, duration of condition, and the number of comorbid pain conditions. Model 4 included all variables from previous models with the addition of experimental pain sensitivity testing results: thermal tolerance, pressure pain threshold of the trapezius, pain rating of mechanical stimulus, and mechanical stimuli windup.

Akaike Information Criterion (AIC) and Bayesian Information Criteria (BIC) were used to compare model fit. The AIC provides information about goodness of fit among these models. The BIC penalizes for more variables in the model and thereby complements the AIC by addressing the potential estimate inflation as the number of parameters increases. The model with the lowest BIC can be interpreted as the model with the maximum posterior probability[37]. The model with the highest cross-validated AUC represents the best model for discriminating between people with low- or high-impact pain. We considered an increase in AUC equal to or greater than 0.05 to indicate a substantial change. Deleting variables and assessing the AUC for change in estimate quantified the role of individual variable contribution to the model. This

process resulted in the selected model (Model 5 in Table 4.4). Statistical significance of the difference between two models was also measured to compare the models.

To address potential sex differences indicated by previous research, the sample was stratified by sex and selected models were re-run in each population. Changes in the AUC between males and females would indicate a need to develop separate models based on sex.

Missing data

Figure 4.1 shows the STROBE diagram of missing data from the sample of 1088 people, resulting in the final complete case sample restricted to 846 people. Participants with any missing data for the variables included in the modeling procedure were excluded from all analyses. Only 4% of the full sample exhibited missing data for the outcome of interest. Sample B shows restriction to the 99% of the sample that had complete data for addressing psychological distress variables (n=13). Sample C is restricted to 95% of Sample B when people with missing data about clinical pain features (n=52) were excluded. The final study sample was 87% of Sample C as the largest exclusion was due to missing experimental pain data (n=131). The percentage of participants with missing data were compared between low- and high-impact pain groups, according to variables used in the analyses. Chi-square tests were used to evaluate differences between groups. Individual items missing from questionnaires were imputed using the expectation-maximization (EM) algorithm in the datasets available for this analysis. OPPERA investigators describe the method in the following way: “In general, if a subject skipped at least 1 but less than half the items in a questionnaire, the missing items were imputed. If they failed to complete at least half of the items in the questionnaire, we treated their summary score as missing”[38].

We used SAS software Version 9.4 of the SAS System for Windows to perform all analyses. Copyright © 2012 SAS Institute, Cary, NC.

3 Results

Descriptive data

One third of the study participants (33.5%) reported characteristics consistent with high-impact pain indicating interference with their day-to-day activities. The mean age of participants was 29.0 years (SD 7.8). The ratio of female to male participants in both categories of disability was 3:1. Over 70% of the sample identified as white, while 14% of the sample identified as Black or African American.

We created tertiles to compare differences in the distribution of people among in high, medium, and low levels of explanatory variables and compared the distributions among people with high-impact pain compared to low-impact pain. Forty-one percent of the low-impact sample was in the 18-24 age range while 30% of the high-impact group was in this age category, indicating older people were more likely to experience high-impact pain. There were race/ethnicity differences by impact with 76% of the low-impact group identifying as white while 62% of the high-impact group was white. Twenty-five percent of the high-impact group identified as Black or African American. Sex distribution by impact was very similar. There were more women than men in the sample of cases, with the 3:1 female to male ratio observed in both low and high-impact groups. People with low-impact pain scored higher on the POMS positive affect scale and lower on the negative affect scale. There were similar patterns for catastrophizing, somatic symptoms, jaw functional limitation, and oral parafunction behavior with the low-impact group demonstrating lower scores and higher scores among the high-impact group indicating a higher level of distress and impairment. Other variables did not present with a

monotonic relationship among the low, medium and high groups. The percentage of people with the lowest number of painful body sites among people with low impact was 35%, then 37% in the medium group and 28% for the highest group while the high impact group was distributed in the low, medium, and high categories at 32, 25, and 45% respectively.

The mean history of orofacial pain was 7.0 years (SD 6.4). Among people with high-impact pain, the mean duration was 7.4 years while the low-impact group had a mean duration of 6.7 years with standard errors of 7.6 and 8.0 years respectively. Approximately 70% reported having ever seen a health care provider for facial pain. Among people with high compared to low-impact the frequency of reported treatment seeking was 76% and 67% respectively (not shown).

Among people with high-impact pain, the mean number of painful body sites was 7 while people with low-impact indicated a mean of 5 sites (rounded to the nearest whole number to represent pain sites). Table 4.2 shows people with low-impact pain reported one less painful condition from the 20 conditions compared to people with high-impact pain. Experimental pain testing results indicated people with low-impact pain demonstrated higher pressure pain thresholds measured on the trapezius, rated the mechanical probe less painful, and had less wind-up with the mechanical probe compared to the high-impact group.

Comparison of models

The initial multivariate model included sociodemographic variables: race, age, sex, and study site. These variables represent the minimum of controlling for study design and sociodemographic characteristics that may be associated with high-impact pain compared to models accounting for multidimensional aspects of high-impact pain. The area under the curve (AUC) of model 1 was 0.61, somewhat better than chance (0.50). Self-reported race was associated with parameter estimates of high-impact pain with individuals identifying as Black or

African American more likely to experience high-impact pain compared to people who identified as white. People who identified as Asian, Hispanic, other or multiple racial or ethnic groups did not have elevated estimates of high-impact pain. There did not appear to be an effect of age or gender. Compared to the Chapel Hill study site, people living in Gainesville had similar odds of high-impact pain while people living in either Buffalo or Baltimore had higher odds of high-impact pain.

Model 2 was comprised of 8 variables: 4 variables from model 1 plus 4 variables representing psychological distress: overall positive affect and negative affect scores from the POMS, the SCL-90R somatization subscale and CSQ-R Catastrophizing subscale score. While the POMS scores seemed to have no contribution to increasing the AUC, increased somatization and catastrophizing scores were associating with increased pain impact.

Model 3 included all variables from model 2 with the addition of 6 variables measuring clinical pain features including the combined global jaw functioning limitation score, oral behavior checklist, jaw opening, number of painful body sites, number of comorbid conditions, and duration of pain. Among the added variables, increases in jaw functional limitation and number of painful body sites were the only variables associated with an increase in impact. Model 4 is the full model, including all variables in model 3 plus the 4 experimental pain testing variables: thermal tolerance, pressure pain threshold, mechanical pain rating, and mechanical pain windup. Although temporal summation of mechanical pain and mechanical pain rating had different means by impact group in univariate analyses, the logistic regression model showed no independent association with high-impact pain.

Based on the findings of the hierarchical model building process, we constructed a parsimonious selected model (model 5) designed to achieve the highest AUC with the lowest

number of variables. This model included sociodemographic variables, catastrophizing, jaw limitation, and painful body sites. Though age and gender were not associated with impact, these variables were retained in the selected model because they have been identified as variables of interest in prior research. Also, though somatic symptoms were associated with high impact, removing this variable from the selected model did not cause a reduction in the AUC. Table 4.5 shows the results from all 5 models and figure 4.2 shows all curves. Despite overlap in the 95% confidence intervals for AUC from models 2, 3, 4, and the selected model, the chi-squared p-value comparing model 4 to the selected model and model 3 to the selected model were not statistically significant (p=0.83 and p=0.64 respectively).

Because models 3 (the model containing all sociodemographic, clinical pain and psychological distress variables) and 4 (the full model) were so similar in cross-validated AUC, we turned to model BIC and AIC to assess model fit. The AIC decreased from 1001 (model 2) to 872 with the addition of clinical variables (model 3). The smaller value, indicating better fit, did not fluctuate much with the addition of the experimental pain sensitivity variables (model 4) or the reduction in variables in the selected model (AIC= 871). The BIC decreased with the addition of mood variables (936), and again slightly with clinical variables (967), but increased with experimental pain variables indicating the penalty for additional variables that did not increase the model fit. The selected model had the lowest BIC (933).

Finally, when we ran models 4 and 5 stratified by sex, we found the AUC from model 5 was identical for both men (n=194) and women (n=652). When model 4 was performed with sex stratification, the differences were in the third decimal place (women AUC=0.7717 and male AUC=0.7752).

Missing data results

Approximately one fifth of subjects (19%) had incomplete data for one or more variables used in this analysis (Table 4.3). There was some variation in the percentage with incomplete data among racial groups, but no differences by age or sex. The Florida study site had the most complete data. The percentage of people with incomplete data increased as catastrophizing increased ($p=0.03$) and differed according to jaw function ($p<0.0001$), although not in a monotonic manner. There was no statistically significant difference between missing and complete data by positive and negative affect scores, somatization score, oral behavior checklist sum score, maximum unassisted opening, reported duration of pain, pressure pain threshold, or mechanical pain testing.

Frequency of incomplete data varied according to the number of painful body sites and the number of comorbid painful conditions. There was less missing data in the highest thermal tolerance category. In summary, missing data was related to overall increased severity and symptoms, indicating that individuals with more comorbid pain conditions may have been less likely to complete all study components.

Because we performed complete case analysis, the sample was limited to n=846. As the selected model did not include experimental pain testing results which were the variables accounting for the most missing data, the model was repeated using the original sample with missing data only from the variables included in the model. This yielded a sample of n=1014 and an AUC of 0.79, 95% CI (0.76, 0.82) and BIC=1115. The results of multiple imputation for model 4 (the full model) was 0.80 (with individual imputations AUC ranging from 0.79 to 0.80), 95% CI (0.77, 0.83), SE=0.01. These results are nearly identical to results from the complete case analysis. We performed a sensitivity analysis using data from a more complete sample

(Sample B in figure 4.1). The results of the selected model in this larger population (n=1014) were the same AUC. We also performed multiple imputation and we found the AUC measure to be robust.

4 Discussion

Key Results

This is the first large study addressing the distinction between levels of pain impact among community dwelling people with TMD. We found that catastrophizing, jaw functional limitation, and tenderness to body palpation were useful tools for discriminating between high- and low-impact pain. Specifically, people with TMD who reported greater pain catastrophizing, increased jaw limitation, and more painful body sites were more likely to experience high-impact pain than low-impact pain. Our selected model containing sociodemographic variables, catastrophizing, jaw limitation, and painful body sites performed as well as the full model with all 18 variables. The high-performing selected model with 3 major predictors represents a simplified model of high-impact pain focused on 3 unique characteristics that can easily be evaluated in a clinical setting.

Interpretation

It is important to note that, even though we used a predictive modeling approach, the parameter estimates cannot be interpreted as causal as the data is cross-sectional and we have not controlled for confounding. The model building strategy was designed to assess the contribution of variables to the ability to discriminate between high- and low-impact pain, therefore the goal was the highest AUC achieved with the simplest model. Consistent with the TRIPOD statement[39], we have produced the first step in prediction by testing predictive performance in one data set. The large cross-sectional study provided an adequate number of chronic TMD cases

in order to make multiple comparisons by identified variables of interest. The next step for understanding the etiology of pain impact requires a longitudinal setting that should be informed by the findings presented here.

Previous research implicated depression, pain duration, female gender, and somatization[12] as contributors to pain-related disability. We found no effect of gender or pain duration on pain impact. Restricting the sample by sex and running both the full and selected models further explored the effect of gender. These results indicated no differences between men and women in the application of the selected model.

We found Black or African American people were more likely to experience high-impact pain compared to other racial or ethnic categories including Asian, Hispanic, and Caucasian. Previous research has identified racial difference in clinical as well as experimental pain[40]. In univariate analyses, people who identified as Black or African American were older than participants from other racial groups and reported higher scores on catastrophizing and jaw limitation, but not more painful body sites. In a model of pain impact using race as the single predictor, people identifying as Black or African American had 3.5 times the odds of having high-impact pain compared to whites (AUC=0.34, 95% CI (2.4, 5.2)). Univariate findings suggest that African Americans in this sample were more likely to report features that we found associated with high-impact pain. However, the relatively small number of African Americans in the sample (n=120) is a limitation of this finding. Future research is needed to address race inequalities and pain impact to understand this relationship.

Limitations

Due to the cross-sectional nature of the study, the prediction model is diagnostic as opposed to prognostic. The cross-sectional design does not permit conclusions about whether or

not high-impact pain is caused by functional limitation and catastrophizing or if the reverse could be true. The age range of 18-44 is a potential limitation because the sample over-represents younger people with TMD. The narrow age range of participants is likely not representative of the entire population living with chronic orofacial pain. Additionally, there is the likelihood that unmeasured variables could have improved upon the performance of the predictive model. Somatic symptoms were of interest because somatization has been associated with pain-related disability in previous research[41], but the specific measurement of somatization in this study heavily influenced the decision to exclude it from the final model. A randomized controlled trial of 101 community-dwelling people with TMD assessed the effects of cognitive behavior therapy (CBT) at multiple time points after treatment and found somatization moderated the effect of treatment on pain-related interference[42]. That study used the same measure of somatization that we used: the SCL-90R. Our findings are consistent with previous research findings identifying an association with the SCL-90R somatization scale and high-impact pain, but the somatization scale was not included in the final model because the measure did not improve the AUC and other measures of somatization analyzed were not associated with high-impact pain (results not shown).

Missing data were an issue that required careful attention. Our examination of missingness was illuminating in two ways. We observed potential patterns in the data related to missingness and severity of the condition or symptoms. Based on sensitivity analysis and multiple imputation results, we conclude that the AUC is a robust measure that remained unchanged under different approaches to address missingness.

Generalizability

A major strength of this study is the community-dwelling sample. As opposed to a clinical sample recruited from tertiary pain clinics, participants in this study represent varying

levels of treatment seeking and therefore, the results should be generalizable to the larger population of people with painful TMD. Approximately 70% of the sample reported having ever seen a healthcare provider for facial pain. The frequency of reported treatment seeking was 75.9% and 66.6% among people with high- and low-impact pain, respectively. This result points to the conclusion that almost a quarter of people meeting the criteria for high-impact pain reported never having seen a healthcare provider for treatment.

A second strength of our approach is the unique comprehensive assessment of study participants. In addition to self-reported questionnaire data, we were able to include an exploration experimental pain sensitivity testing. The extensive data collection allowed for a very thorough assessment of multiple dimensions that could influence pain outcomes. Although experimental pain testing may have usefulness in clinical practice for identifying subgroups of patients[43] or predicting post-operative pain[44], our results support the conclusion that experimental pain testing has limited ability to differentiate high-impact from low-impact TMD pain.

The Federal Strategy for Pain report says: "*High-impact chronic pain* is associated with substantial restriction of participation in work, social, and self-care activities for six months or more"[45]. The report recommends an assessment of high-impact pain based on the response to 3 questions about how often people experience interference due to pain in "usual work, regular social and recreational activities, and taking care of myself" with the answers never, rarely, sometimes, usually or always. Based on this scale, high-impact chronic pain is defined as at least one of the 3 items rated "usually" or "always". The difference in this proposed method and the GCPS used in our research is the GCPS asks participants to rate extent, rather than frequency, of

interference on the 0 to 10 scale and the GCPS classification is also based on pain intensity and work days missed.

Managing high-impact pain is imperative for clinicians treating chronic TMD. Information about characteristics associated with high-impact pain therefore is valuable clinically for targeting and modification to improve patient outcomes. Several research studies have produced evidence that CBT and biofeedback training may reduce pain impact[25, 46, 47]. For example, patients who received combined CBT and biofeedback training experienced greater change in pain-related disability measured with the GCPS compared to the control group[46]. When "usual treatment" (described as typically physiotherapy, patient education, medications, and occlusal appliance therapy) was compared with usual treatment plus a 6-session cognitive behavioral intervention, researchers found pain-related interference was reduced among those receiving CBT but the benefit was temporary[25]. In a sample of 115 TMD patients, researchers reported pain-related beliefs mediated CBT effects on disability at one-year follow-up[47].

In conclusion, the current study demonstrated an association between catastrophizing, jaw functional limitation, and painful body sites with high-impact pain while gender, duration of condition, and experimental pain sensitivity were not associated with high-impact pain. We found that one third of people with chronic TMD experienced high-impact pain and that catastrophizing, jaw limitation, and painful body sites were associated with high-impact pain while pain duration, gender, and experimental pain sensitivity were not. This finding is consistent with the hypothesis that pain impact is a complex construct associated with clinical pain features as well as ability to cope with pain. Assessing catastrophizing and jaw functional limitation requires two brief questionnaires while assessing painful body sites can be performed with a brief physical exam. Understanding and improved targeting of catastrophizing, jaw

limitation, and body pain for therapeutic intervention is important to reduce the impact of pain among people with chronic TMD.

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Tables

Table 4.1. Demographic and clinical characteristics of the sample of people with chronic TMD.
Pain-related disability classification: high-impact is GCPS II-high, III, IV (n=283) and low-impact is GCPS I and II-low (n=563).

		Low-Impact Pain (n=563)		**High-Impact Pain (n=283)**	
	Total	N	%	N	%
Race/Ethnicity					
White	604	429	76.2	175	61.8
Black/African American	120	49	8.7	71	25.1
Asian	38	29	5.2	9	3.2
Hispanic	56	38	6.8	18	6.4
Other	28	18	3.2	10	3.5
Age (years)					
18-24	314	229	40.7	85	30.0
25-34	305	205	36.4	100	35.3
35-44	227	129	22.9	98	34.6
Sex					
Male	194	126	22.4	68	24.0
Female	652	437	77.6	215	76.0
Study site					
UNC	239	177	31.4	62	21.9
UB	201	122	21.7	79	27.9
UF	237	173	30.7	64	22.6
UMD	169	91	16.2	78	27.6

UNC= University of North Carolina at Chapel Hill; UB=University of Buffalo, NY; UFL=University of Florida at Gainesville; UMD=University of Maryland at Baltimore

Table 4.2. Continuous variables in the sample of people with chronic TMD by pain impact classification

Low-impact is GCPS I and II-low and high-impact is GCPS II-high, III, IV.

	Total		**Low-impact pain**		**High-impact pain**		**Comparison**
	Mean	SD	Mean	SD	Mean	SD	P-value[†]
Age (years)	29.0	7.8	28.2	7.6	30.5	8.0	<0.001
POMS: Overall positive affect[*]	80.7	16.2	82.0	15.8	78.0	16.7	0.008
POMS: Overall negative affect[*]	58.2	18.8	56.0	17.5	62.6	20.4	<0.001
Catastrophizing[*]	0.7	0.6	0.6	0.5	1.0	0.7	<0.001
Somatization[*]	1.4	1.2	1.1	1.1	2.0	1.3	<0.001
JFLS global measure[*]	2.0	1.5	1.6	1.3	2.9	1.7	<0.001
OBC total score[*]	32.8	11.0	31.9	10.2	34.7	12.2	0.001
Maximum unassisted opening (mm)	46.9	8.9	47.3	8.4	46.2	9.8	0.085
Number of painful body palpation sites	5.8	4.0	5.4	3.6	6.6	4.5	<0.001
Number of pain comorbid conditions	2.6	2.6	2.2	2.1	3.6	3.0	<0.001
Duration of pain (years)	6.9	6.4	6.7	6.2	7.4	6.7	0.155
Thermal tolerance (^{o}Celsius)[*]	45.6	2.4	45.7	2.3	45.3	2.5	0.029
Pressure pain threshold: trapezius (kPa)[*]	278.8	125.0	288.5	127.9	259.5	116.7	0.001
Mechanical probe pain rating[*]	11.8	14.8	10.3	11.9	15.0	19.0	<0.001
Mechanical temporal summation[*]	13.4	14.5	12.1	13.0	15.8	16.8	0.001

Abbreviations: POMS, Profile of Mood States: Bi-polar Form; JFLS, Jaw Functional Limitation Scale; OBC, Oral Behaviors Checklist
[*]Variable includes imputation of up to 50% missing items [†]P-value from t-test comparing low- and high-impact pain groups

Table 4.3. Results of binary logistic regression models predicting presence of high-impact pain

	Demographic only	Model 1 + psychological distress	Model 2 + clinical pain features	Model 3 + experimental pain sensitivity	Selected model
Number of subjects	846	846	846	846	846
AUC	0.65	0.76	0.81	0.82	0.80
AUC cross validated	0.61	0.74	0.79	0.79	0.79
95% CI	0.57, 0.65	0.70, 0.77	0.75, 0.82	0.75, 0.82	0.76, 0.82
SE	0.02	0.02	0.02	0.02	0.02
Model BIC	1088.36	935.53	967.32	985.68	932.53
Model AIC	1040.95	1001.90	872.51	871.90	870.90
Race (ref= white)					
Asian	0.92 (0.40, 1.94)	0.86 (0.34, 1.96)	0.99 (0.38, 2.36)	0.86 (0.32, 2.08)	1.00 (0.38, 2.34)
Black	2.83 (1.83, 4.39)	2.64 (1.64, 4.28)	2.74 (1.63, 4.63)	2.39 (1.40, 4.10)	2.72 (1.64, 4.54)
Hispanic	1.24 (0.67, 2.22)	1.19 (0.61, 2.25)	1.24 (0.63, 2.39)	1.09 (0.54, 2.11)	1.22 (0.62, 2.34)
Other	1.38 (0.59, 3.03)	1.32 (0.55, 3.03)	1.36 (0.52, 3.32)	1.23 (0.47, 3.09)	1.39 (0.54, 3.41)
Age	1.02 (1.00, 1.04)	1.02 (1.00, 1.04)	1.02 (1.00, 1.05)	1.03 (1.00, 1.06)	1.02 (1.00, 1.05)
Sex (ref=male)					
Female	1.07 (0.75, 1.54)	1.07 (0.72, 1.60)	0.92 (0.59, 1.45)	0.90 (0.57, 1.45)	0.84 (0.55, 1.30)
Study site (ref=UNC)					
UB	1.68 (1.12, 2.55)	1.29 (0.82, 2.04)	1.35 (0.83, 2.19)	1.48 (0.91, 2.41)	1.35 (0.84, 2.18)
UF	1.06 (0.69, 1.61)	1.04 (0.66, 1.63)	1.18 (0.74, 1.90)	1.14 (0.69, 1.88)	1.16 (0.73, 1.86)
UMD	1.70 (1.09, 2.67)	1.49 (0.92, 2.43)	1.72 (1.00, 2.95)	1.74 (1.00, 3.03)	1.70 (1.00, 2.91)
POMS: Overall Positive Affect*		1.00 (0.99, 1.01)	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)	
POMS: Overall Negative Affect*		1.00 (0.99, 1.01)	1.00 (0.99, 1.02)	1.00 (0.99, 1.02)	
Somatization*		2.04 (1.47, 2.84)	1.54 (1.04, 2.30)	1.52 (1.02, 2.26)	
Catastrophizing*		1.59 (1.37, 1.84)	1.45 (1.24, 1.70)	1.46 (1.24, 1.71)	1.46 (1.25, 1.70)
JFLS Global Measure*			1.63 (1.44, 1.86)	1.63 (1.44, 1.87)	1.59 (1.41, 1.79)
OBC total score*			0.99 (0.98, 1.01)	0.99 (0.98, 1.01)	
Maximum unassisted opening			1.01 (0.99, 1.04)	1.01 (0.99, 1.04)	
Number of painful body sites			1.08 (1.03, 1.13)	1.07 (1.01, 1.13)	1.08 (1.03, 1.13)
Number of comorbid conditions			1.03 (0.95, 1.13)	1.02 (0.94, 1.12)	
Duration of pain (years)			1.00 (0.97, 1.03)	1.00 (0.97, 1.03)	
Thermal tolerance (^{o}Celsius)				0.99 (0.92, 1.08)	
Pressure pain threshold*				1.00 (1.00, 1.00)	
Mechanical probe pain rating*				1.01 (0.99, 1.02)	
Mechanical temporal summation*				1.02 (1.00, 1.03)	

Abbreviations: AUC, Area under the curve; CI, confidence interval; BIC, Bayesian information criteria; AIC, Akaike information criteria; UNC, University of North Carolina at Chapel Hill; UB, University of Buffalo, NY; UF, University of Florida at Gainesville; UMD, University of Maryland at Baltimore, POMS, Profile of Mood States: Bi-polar Form; JFLS, Jaw Functional Limitation Scale; OBC, Oral Behaviors Checklist; kPA, kilopascals

* Variable includes imputation of up to 50% missing items

Table 4.4. Comparison of models

ROC Model	AUC	SE	LCL	UCL	BIC
Model 1 (4 variables)	0.6118	0.02	0.57	0.65	1088.36
Model 2 (8 variables)	0.7360	0.02	0.70	0.77	953.53
Model 3 (14 variables)	0.7853	0.02	0.75	0.82	967.32
Model 4 (18 variables)	0.7861	0.02	0.75	0.82	985.68
Selected model (7 variables)	0.7873	0.02	0.76	0.82	932.53

Model 1 includes race, age, gender, and study site. Model 2 includes model 1 variables and mood variables. Model 3 includes model 2 variables and clinical jaw features. Model 4 includes model 3 variables and experimental pain testing. Selected model includes model 1 and JFLS, catastrophizing, and number of painful body sites.

Figures

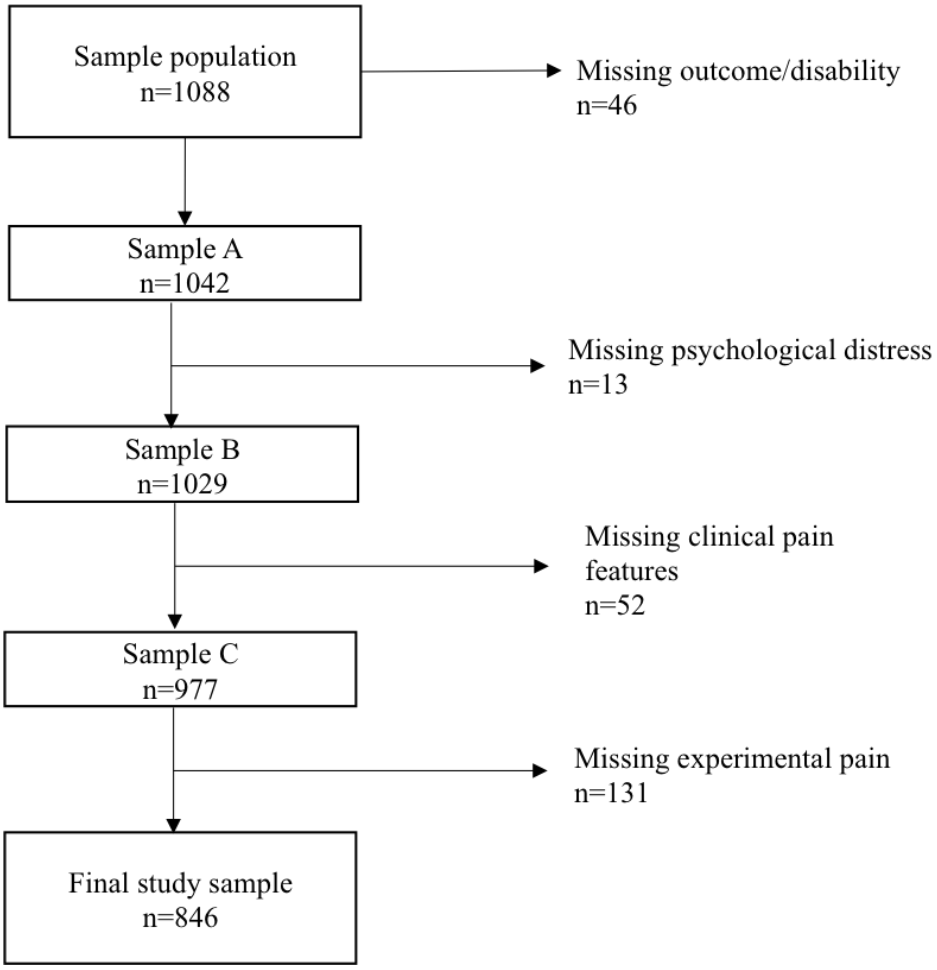

Figure 4.1. Diagram showing exclusion of missing data by domain

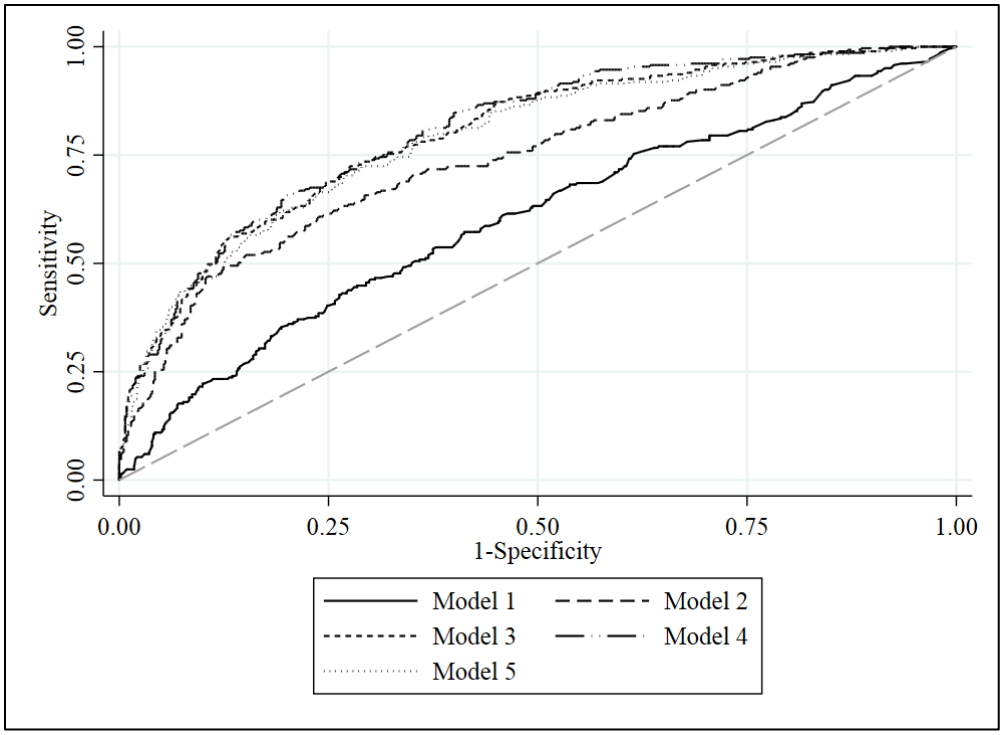

Figure 4.2. The cross-validated AUCROC comparing the selected model to models with demographic variables and patient characteristics.

The full model is shown as the first model, represented by a solid line. Model 1 includes race, gender, age, and study site. Model 2 includes demographics plus mood variables. Model 3 includes demographics plus mood and clinical variables. The selected model includes race, age, gender, study site, catastrophizing, JFLS score, and number of painful body sites.

Supplemental material

Table 4.S.1 Demographic and clinical characteristics of the sample with complete (n=846) and missing data (n=196)

	N with complete data	% with incomplete data	P-value
Impact			
Low	563	16.7	
High	283	22.7	0.02
Race/Ethnicity			
White	604	18.2	
Black/African American	120	26.4	
Asian	38	11.6	
Hispanic	56	12.5	
Other	28	17.7	0.05
Age (years)			
18-24	314	15.6	
25-34	305	19.5	
35-44	227	22.0	0.10
Sex			
Male	194	18.5	
Female	652	18.9	0.88
Study site			
UNC	239	26.9	
UB	201	17.3	
UF	237	9.5	
UMD	169	19.5	<0.0001
POMS7: Overall Positive Affect[*†]			
Low (0-72.9)	263	19.8	
Medium (73.0-87.9)	276	17.9	
High (88.0-120.0)	307	18.6	0.81
POMS8: Overall Negative Affect[*†]			
Low (0-46.9)	283	17.3	
Medium (47.0-64.9)	278	17.8	
High (65.0-120.0)	285	21.1	0.27
Somatization[*†]			
Low (0.-0.3)	297	15.6	
Medium (0.4-0.8)	251	19.8	
High (0.9-4.0)	298	19.0	0.34
Catastrophizing[*†]			
Low (0-0.6)	275	14.1	
Medium (0.6-1.8)	274	18.7	
High (1.8-6.0)	297	22.3	0.02
JFLS Global Measure[*†]			
Low (0-1.16)	286	17.1	
Medium (1.17-2.6)	298	11.3	
High (2.7-10.0)	262	24.7	<0.0001
OBC total score[*†]			
Low (0-27.0)	276	16.6	
Medium (27.1-36.9)	274	18.0	
High (37.0-84)	296	20.1	0.33

Maximum unassisted opening[†] (MM)			
<44	279	19.1	
44-51	278	13.9	
>51	289	18.8	0.14
Number of painful body palpations sites[†]			
0-3	286	14.1	
4-7	279	14.2	
8-14	281	24.3	0.0002
Number of pain comorbid conditions[†]			
0	199	14.2	
1-3	411	16.1	
4-20	236	21.6	0.05
Duration of pain[†] (years)			
0-2.9	304	18.7	
3-7.9	244	18.9	
8.0-35.0	298	18.8	0.99
Thermal tolerance[*†] (^{o}Celsius)			
0-44.8	267	17.1	
44.9-46.6	295	12.1	
46.7-53.0	287	10.0	0.02
Pressure pain threshold Trapezius[*†] (kPa)			
0-202.2	272	14.7	
202.3-303.7	278	12.6	
303.8-600.0	296	10.6	0.28
Mechanical probe pain rating[*†]			
0-3.0	273	15.5	
3.1-11.1	279	16.7	
11.2-100	294	15.5	0.88
Mechanical windup[*†]			
-13.7-4.6	281	14.6	
4.7-13.6	267	18.6	
13.7-85.0	298	14.6	0.27

[*]Denotes variable includes imputation of up to 50% missing items. [†]Categorical variable delineations refer to tertiles. P-value is from the chi-square test that the percent of complete data is the same in groups

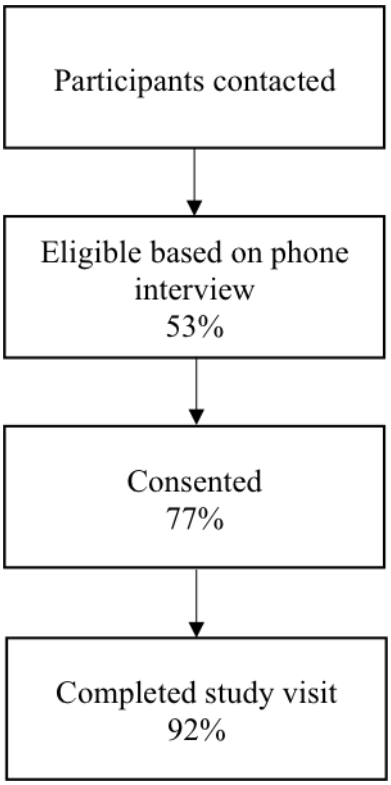

Figure 4.S.1. Recruitment flowchart of 896 participants with chronic TMD enrolled between 2011 and 2013.
This sample was used to supplement the original 192 chronic cases that were enrolled in the initial study period beginning in 2006.

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CHAPTER FIVE: EXPLORING THE RELATIONSHIP BETWEEN FACTORS ASSOCIATED WITH PAIN-RELATED DISABILITY IN PEOPLE WITH PAINFUL TMD: A STRUCTURAL EQUATION MODELING APPROACH

Overview

Background: Pain-related disability is a sophisticated construct that refers to impact on individual functioning and can fluctuating based on unknown factors. Disability is common among people with chronic temporomandibular disorder (TMD). The purpose of this research was to examine the relationship between factors associated with pain-related disability among people with chronic TMD.

Methods: We conducted a cross-sectional analysis of a community-based sample of 1088 individuals with chronic TMD who had complete data. We re-validated a measure of pain-related disability and created measurement models of TMD clinical features, psychological distress, and experimental pain sensitivity. Latent variables were combined for a full structural equation model that was modified using exploratory model changes.

Results: Participants were 18-44 years old (mean 29.2, SD $\pm$ 7.8) with a mean duration of 6.9 (6.4) years of chronic TMD pain. A model of pain related disability, TMD features, and psychological distress was created and refined based on exploratory model revisions. Estimation of the final model indicated a good fit with the data. TMD clinical features and psychological distress predicted pain-related disability but experimental pain sensitivity did not. The final model explained 78% of the variance in pain-related disability.

Conclusions: TMD clinical features (specifically jaw limitation) and psychological distress (including negative affect, somatization, and catastrophizing) should be considered by clinicians and researchers addressing pain-related disability.

1 Introduction

Background

Painful temporomandibular disorder (TMD) is defined by localized pain involving masticatory muscles and associated limitation in jaw function. People with TMD report pain in the face, jaw, temple, and ear. The National Health and Interview Survey (NHIS) estimated the prevalence of TMD-like pain in the US population at 4.6%, based on data pooled from 2000-2005[1]. The experience of living with jaw pain can involve not only discomfort but also distress from its effect on everyday life, including work and social restrictions[2]. The negative impact of living with temporomandibular disorder pain on quality of life has been well established[3, 4].

Research addressing the prevalence of other pain conditions among people with TMD and the systemic nature of impairment among people with painful TMD supports the conclusion that while TMD is defined by jaw pain, the personal experience likely involves comorbid pain conditions that compound impairment. For example, NHIS data from 2000-2005 found that more than 99% of those with TMD-like pain also reported comorbid headache/migraine, neck, or lower back pain, and nearly 59% reported having at least two more areas of severe pain[1].

Disability

The task of defining and measuring health-related disability has a long history in medicine, psychology, sociology, and other disciplines. There is extensive literature exploring the meaning of disability and its economic, legal, and social implications. Here, we explore the

subjective experience of disability, drawing on the classic definition by Nagi[5] (1965) that explores people's ability to fulfill "socially defined roles and tasks within the environment." Nagi's model (shown in figure 5.1) distinguishes disability from functional limitation, pathology, and impairment while acknowledging the interrelationships between the concepts.

Other conceptual models of disability

The World Health Organization (WHO) first published the International Classification of Impairments, Disabilities, and Handicaps (ICIDH) in 1980, presenting a framework for classifying the consequences of disease. Like the Nagi model above, the ICIDH model (shown in 5.2) does not include pain as a factor in the depiction of disability.

Definitions of the key concepts in the model are shown in Table 5.1 and are similar to Nagi's conceptual definitions. In contrast to Nagi's model, the 1980 ICIDH model contains only single-headed arrows, indicating that impairment leads to functional limitation, which leads to disability. The Nagi model has a more dynamic approach, recognizing that pathology, impairments, limitations, and disability can influence one another in bidirectional and nonlinear relationships among variables.

In 2001, the WHO published the International Classification of Functioning, Disability and Health (ICF)—replacing the ICIDH as the "framework for measuring health and disability at both individual and population levels" (http://www.who.int/classifications/icf/en/)[6]. In this publication, the ICF eliminated the term 'handicap' and made broad changes to incorporate the biopsychosocial framework of health as opposed to the medical or social models that do not take into account the interplay between health and social roles. Figure 5.3 shows the revised model published by the WHO in 2001. This model contains double-headed arrows denoting the complex relationships among impairments, limitations, and restrictions and indicating health

conditions can be influenced by limitations. This model represents a substantial improvement from the 1980 model with the exclusion of the term 'handicap' and the recognition of interrelatedness between impairment, limitations and restriction. Additionally, the 2001 model comes closest to the original Nagi model in terms of related concepts.

In my opinion, the conceptual diagrams do not require a separate construct representing pain, particularly since pain can be defined as an impairment, a disease in itself, and/or a factor that influences limitations and restrictions. However, this can lead to confusion since the ICF reference framework links questions about pain interference to the concept "pain as a body sensation"[7, 8] indicating pain interference is a symptom or a consequence of disease or a health condition. When applying the ICF framework to chronic pain conditions, it should be noted that when chronic pain is the health condition being modeled, then impairment, restriction, environmental factors, and personal factors might influence the severity of pain symptoms.

Disability and TMD

Disability associated with TMD has been studied using a variety of constructs: oral health related quality of life, interference in daily activities, functional limitation, and activities of daily living. In this study, we selected the most widely used measure of pain-related disability that is well validated and reliable: the Graded Chronic Pain Scale (GCPS). Two factors influenced the decision to use this measure: the generalizability and use of this scale in chronic pain populations other than TMD and the National Pain Strategy's recommendation for use of a chronic pain screening that assesses chronic pain severity and interference[9].

The GCPS was developed to measure the extent to which pain is perceived as intense and/or interfering by the patient and the degree to which the pain is disabling[10]. The GCPS consists of 3 domains: characteristic pain intensity, interference, and disability days.

Characteristic pain intensity (CPI) includes the average, current, and worst pain rated using the 0-10 Visual Analogue Scale (VAS). Pain intensity is measured as 0 to 10, with 0 representing 'no pain' and 10 referencing 'pain as bad as it could be'. Interference is rated from 0 (no interference) to 10 (unable to carry on any activities) in three areas of life: 1) daily activities, 2) social, family, and recreation, and 3) work activities. Disability days are calculated using a question about the number of days in which pain prevented participation in daily activities. These three domains and their subscales are combined to represent a "chronic pain grade" from 0 (no pain) to IV (high disability and high pain intensity)[11].

Among people with orofacial pain, high pain-related disability is associated with increased healthcare spending quantified by an average increase of £366 ($444 USD) over 6 months when moving from a low to high GCPS category[12]. However, the causes of pain-related disability among people with orofacial pain are not understood. By improving understanding of factors associated with pain-related disability, we can create better interventions to improve or prevent pain-related disability among people with TMD.

Previous studies

Previous research has identified associations between psychological functioning and pain-related disability among people with TMD. Specifically, catastrophizing[13-15], depression[16-18], and somatization (physical symptoms thought to be related to anxiety)[19, 20] are associated with increased disability.

Structural equation modeling was used because the constructs of disability, psychological distress, jaw features, and experimental pain sensitivity all refer to characteristics that are not directly observable. Instead, we use latent constructs comprised of self-reported questionnaire data, physical examination, and laboratory testing to capture data representing these variables.

Structural equation modeling (SEM) is a useful tool for analysis because it allows the researcher to create latent variables representing constructs that cannot be directly observed. The constructs and relationships shown in the ICF model can be analyzed using latent variables. Latent variables can include measured variables such as items on a questionnaire or a summary score that we believe measures the construct of interest. Confirmatory factor analysis (CFA) is used to determine if observed data fit a defined model.

Several research studies have used SEM to examine the relationships depicted in the WHO ICF model[21-25]. In a longitudinal setting, researchers tested temporal relationships among physical impairment (pain), activity and participation restrictions in a sample of 931 people who underwent hip or knee joint replacement assessed pre-surgery and at multiple time points up to 12 months post-surgery. The findings supported the conclusion that both within and across time, pain was associated with activity limitation and activity limitation was associated with participation restriction. This was illustrated by a well-fitting SEM identifying standardized coefficients among pain, activity limitation and participation after adjusting for age, sex, type of surgery, obesity, low back pain, and mood[21]. Another longitudinal study (this one of 548 patients with knee osteoarthritis) found feedback pathways between the ICF components indicating that participation restriction at baseline was predictive or activity limitation 3 years later. This same study using CFA and SEM found mental health to be a mediating factor of the effect of activity limitation on participation restrictions[22].

Only a few studies to our knowledge have explored variables associated with pain-related disability among people with TMD. Our study was primarily concerned with the relationship between physical position of the temporomandibular joint (such as disc displacement) and TMD impact. The authors created a model of the relationship between the physical position of the

temporomandibular joint and TMD impact, which was a latent variable, measured by: 1) observed pain intensity, 2) jaw limitation, and 3) disability. The authors found that these three observed variables had strong and precise loadings on the latent TMD impact measure indicating pain intensity, indicating the JFLS score and disability points from the GCPS together were a useful way to measure impact of TMD. The primary finding was disc displacement is not related to TMD impact[26]. This finding suggests the need to look further than physical features to understand the impact of TMD pain.

The second study was a cross-sectional analysis of 399 people with three types of pain including myofascial pain syndrome. Participants completed the Multidimensional Pain Inventory, the Beck Depression Inventory, and the Minnesota Multiphasic Personality Inventory-2. These observed variables were used to create latent variables representing pain impact, illness conviction, and depression. SEM results supported a causal pathway demonstrating depression predicted illness conviction and pain impact[27]. Davis created five measurement models (including one for psychological distress) and tested a full SEM with an additional observed variable. The results from this cross-sectional study of 251 masticatory muscle pain patients included a well-fitting model with significant associations between variables representing stressors, psychological distress, arousal, sleep problems, and pain symptoms and no association between oral parafunction and pain symptoms[28]. The model published by Davis et al. is shown in figure 5.4. In this model, pain-related disability is not measured, but depression, anxiety, and affective distress were combined to create a latent variable representing psychological distress and the latent variable ‘pain symptoms’ was based on pain severity and visual analog pain ratings.

Objectives

In the present study, we aimed to empirically investigate the relationship between psychological distress, TMD clinical features, and experimental pain sensitivity and pain-related disability. Data from a cross-sectional study of people with chronic TMD were analyzed using SEM to test the variables that were associated with pain-related disability. Our hypothetical model is shown in figure 5.5. On the left side of this model are indicators of psychological distress comprised of four self-reports using standardized instruments, clinical jaw features measured by self-reports, and clinical assessments and experimental pain sensitivity assessed by four quantitative sensory tests. The right side of the model shows the components of the graded chronic pain scale. We hypothesized that pain-related disability would be positively associated with increased psychological distress, functional limitation, and experimental pain sensitivity. This finding would indicate a strong association between the variables we created based on Nagi's model and pain-related disability (shown in figure 5.6).

SEM with latent variables accounts for correlated measures measurement error and has the benefit of examining multiple relationships simultaneously. Latent variables are useful tools to capture the information obtained from observed variables and concurrently account for the different influence each observed variables imparts on the underlying construct (the latent variable)[29].

2 Methods

Sample description

This cross-sectional study of 1088 people with chronic painful TMD examined the relationship between pain-related disability and psychological distress, clinical jaw features, and experimental pain features. Data were available from the parent study, the Orofacial Pain:

Prospective Evaluation and Risk Assessment (OPPERA) study that was conducted between May 2006 and October 2013. The OPPERA study included a case-control study that compared chronic TMD cases with TMD-free controls. Data for the current study are restricted to the 1088 chronic TMD cases enrolled in the parent OPPERA study. For more detail about the OPPERA study protocol and procedures, see Slade et al., 2011[30]. Human Research Ethics Committees at all study sites approved the study protocol. All participants signed an informed consent for study participation and were compensated for their time.

Participants

Participants were community dwelling individuals with chronic TMD who responded to advertisements for people with chronic jaw pain at one of four study sites (University at Buffalo, NY; University of Florida Gainesville, FL; University of Maryland in Baltimore, MD; and University of North Carolina at Chapel Hill, NC). Participants were aged 18-44 years and were required to be fluent in English. Demographic characteristics of the study sample are shown in Table 5.2.

Exclusion criteria were recent facial surgery or facial injury, pregnancy, orthodontic procedures, and major medical conditions including kidney disease or uncontrolled hypertension[30]. Participants completed a telephone interview to assess eligibility prior to completing a battery of questionnaires about health, pain, and psychological functioning and a 3-hour clinic visit that included clinical examination for verification of TMD and experimental pain testing. Chronic TMD was defined as self-reported facial pain symptoms for at least 6 months prior to enrollment AND fulfillment based on examination criteria described below. The 6-month threshold is consistent with the definition of chronic pain provided by the Institute of Medicine: “Chronic pain, by contrast, lasts more than several months variously defined as 3 to 6

months, but certainly longer than “normal healing”[31]. To meet examination criteria for chronic TMD, participants had to experience pain in response to either jaw movement or palpation in at least 1 of the TMJs or at least 3 masticatory muscles[30].

Variables used for SEM

The measures included a mix of self-reported questionnaire responses, clinical measurements of jaw opening and body pain, and experimental pain sensitivity testing results. Table 5.3 shows each measurement and instrument included in measurement model creation.

Pain-related disability

The outcome of interest was pain-related disability, which was measured using individual items from the Graded Chronic Pain Scale (GCPS). The GCPS contains 7 items to assess characteristic pain intensity, interference in daily activities, and disability days (days with decreased or impaired functioning). All questions use the past 6 months as the frame of reference[32]. Characteristic pain intensity was assessed with three questions using the 0-10 pain rating scale. Participants were asked to rate their current pain, worst pain, and average pain over the past 6 months. Participants were asked to rate the extent that pain interfered with their daily activities, recreation, social and family activities, and work (including housework). The rating scale was 0 to 10, where 0 represented “no interference” and 10 was defined as “unable to carry on any activities”. Participants were asked two questions about days of interrupted activity. The first question asked “approximately how many days in the past 6 months have you been kept from your usual activities (work, school or housework) because of facial pain?” The second question is not part of the graded chronic pain scale but offers important information about “presenteeism” and pain impact. Presenteeism refers to lost of productivity at work or on-the-job impairment and is associated with catastrophizing among people with orofacial pain while

absenteeism or work missed is associated with pain severity[33]. The question was “How many days has your efficiency dropped below 50% of what you consider “normal” for you because of facial pain?” using phrasing that referred to all activities and not only job performance.

Psychological distress

Psychological distress was measured using positive and negative affect scales from the Profile of Mood States-Bipolar (POMS-Bi)[34], somatization subscale from the Symptoms Checklist 90-Revised (SCL-90R)[35], and the catastrophizing subscale of the Coping Strategies Questionnaire (CSQ-R)[36].

Clinical TMD features

These were assessed using measured jaw opening, number of painful body sites, oral parafunctional behaviors, jaw functional limitation, number of comorbid conditions, and duration of TMD pain. Instructions for the measured jaw opening measurement was “Open as wide as you can even if you feel pain or increase any pain you are feeling” and opening distance was measured in millimeters. The number of painful body sites was measured by applying pressure to 7 sites bilaterally including the trapezius, supraspinatus, second rib, lateral epicondyle, medial gluteus, greater trochanter, and medial knee[37]. The respondent reported pain or no pain at each site for a sum score from 0-14. Oral parafunctional behavior was measured with the Oral Behavior Checklist (OBC) summary score[38]. The Jaw Functional Limitation Scale (JFLS) measured limitations in three areas: chewing limitation, opening limitation, and verbal or emotional expression[39]. Comorbid conditions were assessed by asking participants a question about the presence or absence of 20 conditions: joint disease or arthritis, fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, tendency to faint, ringing in ears, periodic heart racing or pounding, repeated trouble with neck, back, or spine, insomnia, depression, panic

disorder, post-traumatic stress disorder, anxiety disorder, acid reflux, interstitial cystitis, prostatitis, multiple chemical sensitivity, dysmenorrhea, chronic pelvic pain, and sleep apnea. We used a sum score ranging from 0-20 corresponding to the number of conditions endorsed by participants. We assessed TMD pain duration through self-reports of when their facial pain began.

Experimental pain sensitivity

Experimental pain sensitivity included measures of thermal tolerance, mechanical pain rating of a flat-tipped probe, temporal summation of mechanical probe, and pressure pain thresholds evaluated at the trapezius muscle. Full details of experimental testing procedures are described in Greenspan, 2011[40].

Statistical analysis

Completeness of data, mean, minimum, and maximum variables were analyzed and are shown in Table 5.4. All analyses were performed using the Mplus software, version 8.0[41]. After generating univariate statistics to summarize the data, we conducted three separate analyses. First, we re-validated the GCPS with the inclusion of the question asking about decreased efficiency. Second, we performed confirmatory factor analysis (CFA) to create latent variables representing: 1) psychological distress, 2) clinical TMD features, and 3) experimental pain sensitivity. Finally, we performed a full SEM to examine the relationships between the three latent variables we created and the variable representing pain-related disability.

Structural equation modeling

Robust maximum likelihood was used to address non-normality of variable distribution. Models were evaluated first by assessing parameter estimates and subsequent elimination of variables with low parameter estimates. Then model fit was evaluated based on established

guidelines for goodness of model fit described below. Model fit was assessed using two absolute fit indices: Chi-square test of model fit and root mean square error of approximation (RMSEA). The RMSEA tells us how well the model, with unknown but optimally chosen parameter estimates, would fit the population's covariance matrix. Incremental fit indices included the comparative fit index (CFI) and Tucker-Lewis Index (TLI), both of which account for sample size and performance of the model[42]. Criteria for the model fitness was based on established values for fit indices: CFI/TLI values ≥ 0.95, an RMSEA <0.07[43]. After verifying the fit of each CFA, we built a full structural equation model and performed post-hoc exploratory analysis to improve the fit based on the above criteria for goodness of fit. Variables were eliminated from models where standardized parameter estimates were low (less than 0.3) or when the standardized parameter estimates were not statistically significant ($p>0.05$). Variable removal was performed individually and exploratory analysis continued with deleting variables from the model until the model demonstrated good fit. Code of the SEM analyses is reported in the Supplementary Material section.

Re-validating the GCPS: assessing pain-related disability

In order to determine validity with the observed variable assessing presenteeism, we needed to compare the model without with variable and a model that includes the presenteeism. We compared two first-order models: one with the 7 traditionally used GCPS items and a second model including the variable measuring presenteeism. This is simplistic because ideally, the GCPS is a second-order confirmatory factor analysis but with only the one variable representing participation, we are unable to create a latent concept for participation based on multiple observed variables. Based on that result, we inspected parameter estimates and goodness of fit statistics to determine the validity of the inclusion of the presenteeism variable. If the fit statistics

did not reflect a poorer fitting model, then based on the theoretical framework and conceptual model, we proceeded to validate a second-order confirmatory factor analysis (CFA) of the GCPS with latent variables for pain intensity, interference, and participation. A second-order CFA is distinguished from a first-order in that the second-order CFA involves creation of latent variables comprising another latent variable. For illustration see figure 5.7.

We performed second-order confirmatory factor analysis (CFA) based on the established structure of the GCPS with an additional variable loading on the "participation" latent variable. The latent variable of pain-related disability was comprised of three contributing latent constructs: characteristic pain intensity, pain interference, and participation. The characteristic pain intensity latent variable was expressed by three factors: average, current, and worst facial pain. The interference latent variable was comprised of interference in daily, social and work activities. The participation latent construct was operationalized using number of days of work missed and number of days efficiency dropped below 50% due to pain.

Measurement models

Clinical pain features

We started with a model that included the following eight observed variables: the JFLS chewing limitation score, JFLS opening limitation score, JFLS expression limitation score, maximum unassisted jaw opening from the clinical examination, count of 20 common comorbid conditions, self-reported duration of pain, OBC sum score, number of painful body sites.

Psychological distress

We began with a model that included the following four observed variables: 1) the catastrophizing subscale, 2) the somatization scale, 3) positive and 4) negative affect scales.

Experimental pain sensitivity

We built a model using the latent variable experimental pain sensitivity with the factors of heat pain tolerance, pressure pain threshold, mechanical pain rating, and mechanical temporal summation.

Full SEM

To explore the relationships between the latent constructs of clinical pain features, psychological distress, experimental pain sensitivity, and pain-related disability we built a full SEM regressing the validated measurement models of pain-related disability onto the models described above. We also regressed sex, age, study site, and race onto pain-related disability based on previous research about both pain-related disability and pain severity. The model was evaluated based on parameter estimates and model fit indices described above. Exploratory changes to the model were based on parameter estimates as described above. Modification indices calculated by Mplus indicated when model fit could be improved by accounting for correlation among variables. Additionally, we restricted the sample by sex and re-ran the final model to examine potential sex differences in model performance.

3 Results

Demographics

The mean age among participants was 29.2 years (7.8 SD) with a mean duration of pain of 6.9 years (6.4 SD). 70% of participants were white and 76% of participants were female. There were more people enrolled at the Chapel Hill study site; the Baltimore study site enrolled the fewest participants. Table 5.2 shows characteristics of the study sample. Table 5.4 lists each latent variable with the observed variables, the number of participants with complete data for

each variable, and the mean, minimum, and maximum values for each variable. Demographic data were collected upon entry: age, self-reported sex, self-identified racial identity, and study site. Demographic variables were control variables regressed onto the outcome variable to account for demographic and study site influences on the outcome. Participants rated their current facial pain at a mean of 3.8 (2.5 SD) using the 0 to 10 scale, while the mean worst facial pain in the past 6 months was 7.5 (2.0 SD). The "disability days" variables had a non-normal distribution with 50% of the sample reporting they did not experience any days when they were kept from their usual activities because of facial pain. Reduced efficiency was more common with 25% of the sample reporting 35 or more days during which their efficiency dropped below 50% of what they considered to be normal.

Exploratory modeling results

Results from the measurement models of pain-related disability with and without the variable measuring presenteeism were compared. The first-order 7 variable model had poor fit (RMSEA=0.219, 90% CI for RMSEA (0.206, 0.233), CFI =0.749, TLI=0.624, SRMR=0.108). The first-order model with 8 variables demonstrated slightly better fit (RMSEA=0.192, 90% CI for RMSEA (0.181, 0.204), CFI =0.752, TLI=0.653, SRMR=0.105) than the model without the presenteeism variable.

This result from the 8 variable model justified the creation of the second-order confirmatory factor analysis (see figure 5.8). The standardized parameters show the highest contribution from the interference latent variable (0.88), the participation latent variable had a high loading (0.83) and the pain intensity latent variable was strong and significant but a lower value (0.65) than the other two latent constructs. This re-validated GCPS model demonstrated excellent fit (Chi^2= 62 ($p<0.0001$), df=17, RMSEA=0.050, 90% CI for RMSEA (0.037, 0.063),

CFI =0.986, TLI=0.977, SRMR=0.021). These results supported the validity of this revised GCPS model.

Measurement models

The full measurement model based on our hypothesized model assessing TMD clinical features demonstrated a poor fit. Subsequently, variables were eliminated from the model when standardized parameter estimates were less than 0.03 (comorbid conditions, duration of pain and OBC score) or did not have a p-value supporting a significant contribution to fit (number of body sites reporting pain).

The model building process with model fit indices and parameter estimates are shown in tables 5.5 and 5.6 respectively. The measurement model of clinical TMD features was reduced to a simplified model containing 3 variables: JFLS subscores measuring opening, chewing, and expression limitation. The measurement model representing psychological distress demonstrated adequate fit after accounting for correlation between the positive and negative affect scales.

The model fit for the experimental pain sensitivity latent variable was good. All factors met statistical significance criteria. The factor loading reflected a positive relationship for heat pain tolerance and pressure pain threshold and a negative relationship for mechanical pain rating and mechanical temporal summation. The well-fitting finalized measurement model containing all three latent variables (clinical TMD features, psychological distress, and experimental pain sensitivity) is shown in figure 5.9.

A four-factor model was proposed to measure psychological distress defined by the following indicators: somatization, catastrophizing, positive and negative affect. The fit of this model was improved after the removal of the positive affect variable. An eight-factor model was proposed to measure clinical TMD features using the following indicators: opening limitation,

chewing limitation, expressional limitation (all from the JFLS), the OBC sum score, measurement of jaw opening, number of painful body sites, and duration of pain. Duration, number of comorbid conditions, OBC score, jaw opening, and number of painful body sites did not load well (standardized parameter estimates less than 0.3) on the latent factor. We systematically removed these variables one at a time in an exploratory process that resulted in a reduced three-factor model restricted to the three subscales from the JFLS. Fit indices for the final exploratory measurement model demonstrated very good fit shown in figure 5.9 (Chi^2= 93 ($p<0.0001$), df= 30, RMSEA= 0.044, 90% CI for RMSEA (0.034, 0.054), CFI = 0.969, TLI= 0.953, SRMR = 0.036).

Structural relationships

The above measurement model result met the criteria specified in the methods section for goodness of fit, permitting the next step of building the full structural equation model. Based on the measurement model results, we proceeded to fit a SEM of pain-related disability regressed onto latent variables representing psychological distress, jaw pain features, and experimental pain sensitivity. Table 5.7 outlines the model-fitting process and the respective fit indices for each alternative model. The initial full model had moderate fit indices indicating improvements in the model specification might improve the fit of the model. To explore and improve fit, we first removed the experimental pain sensitivity latent variable because the standardized parameter estimate (although statistically significant $p<0.000$) was weakly associated with pain-related disability (estimate=-0.171).

Next, we removed observed variables with standardized estimates <0.6: negative affect, positive affect, and maximum jaw opening. The standardized parameter estimates for each step in the exploratory model-building process are shown in table 5.8. Based on the modification

indices, we added acknowledgement of correlation between the latent variables for participation and interference. This adjustment is consistent with the guiding conceptual model for the concepts of jaw functional limitation and pain-related disability. These changes resulted in the final model, which is shown in figure 5.10. The final model demonstrated good fit (fit indices: Chi2= 415 ($p<0.0001$), df= 119, RMSEA= 0.048, 90% CI for RMSEA (0.043, 0.053), CFI= 0.956, TLI= 0.946, SRMR= 0.040) and explained 78% of the variance in pain-related disability.

We controlled for study site, sex, age, and race in the full model. The control variables were used to account for study design and demographic differences in pain-related disability. Jaw limitation and psychological distress had strong loadings on the latent pain-related disability variable (.41 and .58 respectively). Parameter estimate, standardized estimates and p-values for all variables in the final model are shown in table 5.9.

Finally, we ran the final model stratified by sex to examine the potential impact of sex on the whole model. The model fit was good for both men and women and the latent variable loadings were similar. The only difference in significance was that age was not significant in the model restricted to men while age was a statistically significant predictor of pain-related disability although the parameter estimate was low. For both analyses, the psychological distress latent variable had an increased relationship with pain-related disability compared to the jaw functional limitation variable but this relationship was stronger in the analysis restricted to males only (results not shown).

4 Discussion

Key Results

Our results show jaw features and psychological distress have a strong impact on pain-related disability. Psychological distress and jaw functional limitation were both positively

associated with disability. As psychological distress measured by somatization and catastrophizing variables increased, pain-related disability increased. Psychological distress accounted for a higher amount of variance in pain-related disability compared to jaw limitation. In the exploratory model-building process, exclusion of the latent construct measuring experimental pain sensitivity due to low factor loading supports the conclusion that pain testing does not contribute to pain-related disability.

Control variables demonstrated that age, study site, and race were statistically significant predictors of pain-related disability but the parameter estimates for these variables were very low indicating small influence. Control variable parameter estimates were in the expected direction indicating as age increased, pain-related disability increased. Sex was the only sociodemographic variable that was not statistically significantly associated with pain-related disability.

Because controlling for sociodemographic variables on the main outcome variable does not account for potential sociodemographic differences in the latent variables, we performed stratification by sex. When the model was stratified by sex, women compared to men demonstrated similar results, indicating no sex differences among participants in pain-related disability. If there were differences between men and women in the observed variables measuring psychological distress and TMD clinical features, then we would have observed changes in parameter estimates and overall goodness of fit of the models.

Limitations

The primary limitation of this study is the cross-sectional design. In this cross-sectional analysis it is impossible to draw conclusions about causality because there is no temporal component. The SEM approach assumes causality by the use of one-way arrows between exogenous and endogenous variables. When selecting variables to identify in regression models,

we impose a casual structure on the data. There is a need for future research to validate the model reported here in a longitudinal setting.

SEM has multiple strengths that made it the optimal choice for this analysis. SEM permits complex continuous outcome variables, accounts for correlated variables, measurement error, handles missing data well, and performs simultaneous examination of multiple relationships between variables. However, SEM requires strong assumptions that cannot be overlooked. These include the assumption of linear relationships between variables and the assumption of no unmeasured confounding. In this study, there is the possibility that an unmeasured variable caused psychological distress, jaw limitation, and pain-related disability. These assumptions have been cited as a reason for caution when using SEM, particularly the recommendation that SEM is best used when there are many effects being explored for hypothesis generation[44].

Interpretation

As catastrophizing, somatic symptoms, and jaw limitations increased, pain-related disability increased. We can conclude several variables examined did not contribute to pain-related disability. Experimental pain sensitivity, several clinical jaw features including oral parafunction behavior, pain duration, number of comorbid conditions, and the number of painful body sites were all excluded from the model to improve fit. This demonstrates the lack of relationship between the variables listed above and pain-related disability.

Catastrophizing loaded slightly higher than somatization on the psychological distress latent variable indicating that the impact of catastrophizing may be very important in understanding the construct of pain-related disability. This is consistent with previous research about the association between catastrophizing and TMD pain[14, 45-48]. In a cross-sectional

study of a rural chronic pain population, pain catastrophizing was reportedly associated with pain intensity, interference and perceived disability and was found to be associated with perceived disability after controlling for demographics and depression, while depression was associated with pain interference and life satisfaction[49]. Our findings from urban and suburban study sites support the importance of pain catastrophizing consistent with the above finding.

Both psychological distress and functional limitation have been found to be associated with high pain-related disability[18, 20, 50]. This work is the first to model experimental pain sensitivity as a latent construct and examine the relationship between experimental pain sensitivity and pain-related disability. The inclusion of experimental pain sensitivity was based on the biopsychosocial model of pain[51] and the hypothesis that experimental pain testing may measure biological processes such as central sensitization that underlie chronic painful TMD. Research identified somatosensory amplification (increased perception of normal sensation as intensity and/or distressing) among women with chronic orofacial pain[52]. Somatosensory amplification is thought to be a feature common among many pain conditions including fibromyalgia and also among several psychiatric conditions such as anxiety[53]. Although people with TMD have lower pain pressure thresholds[54] and thermal tolerance[55] when compared to pain-free individuals, our finding supports the conclusion that experimental pain sensitivity is not associated with pain-related disability.

Generalizability

Strengths of the study include the large sample size of community dwelling participants with chronic painful TMD. The sample size and recruitment of people from surrounding communities as opposed to specialty pain clinics supports the generalizability of findings to people with chronic painful TMD.

A study of pain-related disability among people with chronic pain conditions including low back pain[56] utilized SEM to model relationships between factors related to disability. Among 156 patients with low back pain, predictors of increased disability included female sex, depression, and fear avoidance beliefs while fulltime employment predicted decreased disability[56]. Our finding contrasts this finding that sex was associated with disability but supports the conclusion that increased depression (measured as negative affect in this study) is associated with increased disability. We did not include assessment of employment status in this study.

Conclusion

We specified and estimated a model based on theory and previous literature to examine factors potentially associated with pain-related disability. This model included latent constructs measuring psychological distress, jaw functional limitation, experimental pain sensitivity, and pain-related disability. We started with a full model and performed modifications based on parameter estimates and model fit indices in order to improve model fit.

The results of this cross-sectional study of people with chronic TMD suggest somatic symptoms, catastrophizing, and jaw functional limitations are important factors to assess in order to understand pain-related disability. Results also demonstrate that experimental pain sensitivity, jaw opening, positive and negative affect scores, duration of pain, and oral parafunction behaviors are not relevant to pain-related disability. After removing the latent construct of experimental pain sensitivity, we simplified the model retaining latent variables measuring psychological distress and jaw functional limitation.

Future research may consider each individual latent structure comprising the GCPS to determine if model fit can be improved upon using individual component of the GCPS. For

example, variables may be more likely to be associated with pain intensity but not interference or vice versa. Future studies should explore this model in other pain populations such as fibromyalgia and migraine headache to explore commonalities and differences among pain populations. The measures in the final model were culled from self-reported instruments making collection of this information straightforward and requiring minimal time or participant burden.

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Tables

Table 5.1. Definitions of concepts used in WHO and Locker models

adapted from Locker 1992 and WHO

Concept	Definition
Impairment	
1988	Anatomical loss, structural abnormality or disturbance in biochemical or physiological proceesses which arises as a result of disease or injury or is present at birth
2001	Problems in body function or structure such as a significant deviation or loss
Functional limitation	
1988	Restrictions in the functions customarily expected of the body or its component organs or systems
2001	Functioning refers to all body functions, activities and participation
Disability	
1988	Any limitation in or lack of ability to perform the activities of daily living
2001	An umbrella term for impairments, activity limitations and participation restrictions
Handicap	
1988	The disadvantage and deprivation experienced by people with impairments, functional limiations, pain and discomfort or disabilities because they cannot or do not conform to the expectations of the groups to which they belong
2001	n/a

Table 5.2. Demographic profile of study participants (n=1088)

Variable	N	Percent
Race		
White	765	70.3
Black	175	16.1
Asian	45	4.1
Other	103	9.5
Sex		
Female	835	76.8
Male	253	23.2
Study Site		
UNC	342	31.4
UB	247	22.7
UFL	271	24.9
UMD	228	21.0

UNC= University of North Carolina at Chapel Hill; UB=University of Buffalo, NY; UFL=University of Florida at Gainesville; UMD=University of Maryland at Baltimore

Table 5.3. Description of each latent variable with instrument and citation

Latent variable name	Observed variable	Instrument	Citation
Psychological distress	Somatization	SCL_90R Somatization scale	Derogatis[35]
	Catastrophizing	Coping strategies questionnaire	Rosenstiel[36]
	Positive & negative affect scores	Profile of mood states-Bipolar	Lorr[57]
Clinical TMD features	Maximum unassisted opening (mm)	Jaw mobility examination	Ohrbach[37]
	Number of painful body sites	Palpation pain examination	Ohrbach[37] & Wolfe[58]
	Oral parafunction behavior	Oral behaviors checklist	Markiewicz[38]
	Chewing, opening, and expression limitation scores	Jaw functional limitation scale	Ohrbach[39]
	Count of comorbid pain conditions & duration of pain	Comprehensive pain and symptoms checklist	Fillingim[37]
Experimental pain sensitivity	Thermal tolerance, pressure pain threshold, mechanical probe rating and mechanical pain summation	Quantitative sensory testing protocol	Greenspan[40]
Pain-related disability	Characteristic pain intensity, interference, and disability	Graded Chronic Pain Scale	Von Korff[32]
	Days efficiency dropped below 50% due to facial pain	Single-item question	Ohrbach[37]

mm=millimeters

Table 5.4. List of observed variables comprising latent variables for measurement models

Variable notation	Latent variable name	Observed variable	N	Mean	Min	Max
PD	Psychological distress	Somatization scale	1073	0.7	0.0	3.1
		Catastrophizing scale	1079	1.5	0.0	6.0
		Positive affect score	1082	80.3	35.0	118.0
		Negative affect score	1082	58.6	30.0	111.0
TMD	Clinical TMD features	Maximum unassisted opening	1069	46.7	8.0	78.0
		Number of painful body sites	1074	6.0	0.0	14.0
		Oral behaviors checklist sum	1079	33	0.0	84.0
		JFLS chewing score	1069	2.5	0.0	10.0
		JFLS opening score	1069	2.7	0.0	10.0
		JFLS expression score	1069	1.2	0.0	10.0
		Count of comorbid pain conditions	1055	2.7	0.0	20.0
		Duration of pain (years)	1070	6.9	0.0	35.0
EXP	Experimental pain sensitivity	Thermal tolerance (^{o} Celsius)	1013	45.4	33.5	51.5
		Pressure pain threshold Trapezius (kPa)	1013	277.6	101.6	600.0
		Mechanical probe pain rating	1047	12.0	0.0	94.8
		Mechanical windup (change in pain rating)	1047	13.3	-13.7	85.0
PRD	Pain-related disability					
CPI	Characteristic pain intensity	Current pain intensity	1062	3.8	0.0	10.0
		Average pain intensity	1062	5.4	0.0	10.0
		Worst pain intensity	1062	7.5	0.0	10.0
INTER	Pain interference	Interference in daily activities	1062	2.5	0.0	10.0
		Interference in social activities	1062	2.4	0.0	10.0
		Interference in work activities	1063	2.2	0.0	10.0
PAR	Participation	Days kept from activities due to facial pain	1054	17.5	0.0	360.0

kPA= kilopascals

Table 5.5. Description and fit indices for measurement models of psychological distress, clinical TMD features, and experimental pain sensitivity

	Description	**N**	**Chi^2 (df)**	**Scaling factor**	**p-value**	**RMSEA (90% CI)**	**CFI**	**TLI**	**SRMR**
Model 1	Full model	1088	1246 (101)	1.077	<0.001	0.102 (0.097, 0.107)	0.669	0.607	0.105
Model 2	Dropped variables with estimates <.4	1088	314 (41)	1.058	<0.001	0.078 (0.070,0.086)	0.886	0.847	0.065
Model 3	Dropped positive affect due to high correlation with negative affect	1088	166 (32)	1.105	<0.001	0.062 (0.053, 0.071)	0.934	0.907	0.051

RMSEA= root mean squared error approximation; CFI= comparative fit index; TLI=Tucker Lewis index; SRMR=standardized residual

Table 5.6. Standardized parameter estimates from 3 models starting with the full model and then performing exploratory model alterations to obtain the best-fitting model

	Model 1	**Model 2**	**Model 3**
Psychological Distress			
Somatic symptoms	0.673	0.660	0.793
Catastrophizing	0.568	0.550	0.608
Positive affect	-0.585	-0.595	
Negative affect	0.768	-0.783	0.615
Clinical TMD features			
Chewing limitation	0.772	0.771	0.773
Opening limitation	0.878	0.887	0.882
Expression limitation	0.721	0.716	0.722
Jaw opening	-0.353		
Number of painful body sites	0.082		
Oral behavior checklist sum	0.213		
Duration of pain	0.082		
Number of comorbidities	0.253		
Experimental pain sensitivity			
Thermal threshold	0.550	0.548	0.542
Pressure pain threshold	0.418	0.413	0.413
Mechanical pain rating	-0.508	-0.512	-0.517
Mechanical temporal summation	-0.449	-0.451	-0.453

Table 5.7. Description and fit indices for 3 models of pain-related disability, clinical TMD features, psychological distress, and experimental pain sensitivity

	Description	N	Chi^2 (df)	Scaling factor	p-value	RMSEA (90% CI)	CFI	TLI	SRMR
Model 1	Full model	1088	833 (193)	1.095	<0.001	0.055 (0.051, 0.059)	0.913	0.898	0.057
Model 2	Dropped EXP	1085	559 (122)	1.080	<0.001	0.057 (0.053, 0.062)	0.935	0.922	0.055
Model 3	Added correlation	1085	415 (119)	1.081	<0.001	0.048 (0.043, 0.053)	0.956	0.946	0.040

df= degrees of freedom; RMSEA= root mean squared error approximation; CFI= comparative fit index; TLI=Tucker Lewis index; SRMR=standardized residual

Table 5.8. Standardized parameter estimates from 3 models starting with the full model and then performing exploratory model alterations to obtain the best-fitting model

	Model 1	**Model 2**	**Model 3**
Characteristic pain intensity	0.708	0.706	0.814
Current	0.713	0.712	0.771
Average	0.871	0.871	0.791
Worst	0.779	0.778	0.683
Interference	0.849	0.851	0.734
Daily	0.883	0.883	0.882
Social	0.907	0.907	0.907
Work	0.904	0.903	0.903
Participation	0.807	0.805	0.689
Days kept from activity	0.741	0.741	0.741
Days less efficient	0.877	0.875	0.875
Clinical TMD features			
Chewing limitation	0.621	0.619	0.643
Opening limitation	0.716	0.714	0.733
Expression limitation	0.883	0.886	0.859
Psychological distress			
Somatic symptoms	0.736	0.736	0.619
Catastrophizing	0.688	0.688	0.734
Negative affect	0.574	0.574	0.421
Experimental pain sensitivity			
Thermal threshold	0.536		
Pressure pain threshold	0.414		
Mechanical pain rating	-0.521		
Mechanical temporal summation	-0.456		
Structural model			
PD→PRD	0.425	0.459	0.578
TMD→PRD	0.388	0.418	0.406
EXP→PRD	-0.199		
Age→PRD	0.117	0.110	0.131
Study site→PRD	0.098	0.096	0.124
Race→PRD	0.030	0.059	0.059
Sex→ PRD	-0.049	-0.009	0.007

PD= Psychological distress; TMD= clinical TMD features, EXP= experimental pain sensitivity; PRD= pain-related disability

Table 5.9. Structural equation model results: association of pain-related disability, psychological distress, and jaw limitation (n=1085)

	Standardized parameter estimate	Standard Error	p-value
Characteristic pain intensity	0.814	0.029	<0.001
Current	0.771	0.021	<0.001
Average	0.791	0.022	<0.001
Worst	0.683	0.023	<0.001
Interference	0.734	0.029	<0.001
Daily	0.882	0.014	<0.001
Social	0.907	0.011	<0.001
Work	0.903	0.012	<0.001
Participation	0.689	0.034	<0.001
Days kept from activities	0.741	0.032	<0.001
Days with reduced efficiency	0.875	0.025	<0.001
TMD clinical features			
Chewing limitation	0.643	0.031	<0.001
Opening limitation	0.733	0.025	<0.001
Expression limitation	0.859	0.024	<0.001
Psychological distress			
Somatic symptoms	0.618	0.033	<0.001
Catastrophizing	0.764	0.034	<0.001
Negative affect	0.421	0.037	<0.001
Structural model			
Psychological distress→PRD	0.578	0.054	<0.001
Clinical TMD features→PRD	0.406	0.053	<0.001
Age→PRD	0.133	0.030	<0.001
Study site→PRD	0.124	0.031	<0.001
Race→PRD	0.059	0.027	0.030
Sex→PRD	0.007	0.030	0.801

PRD= Pain-related disability

Figures

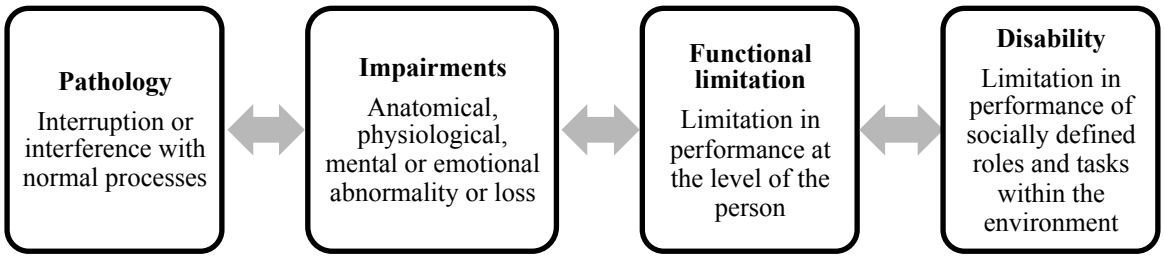

Figure 5.1. Nagi model of disability. Recreated from Nagi

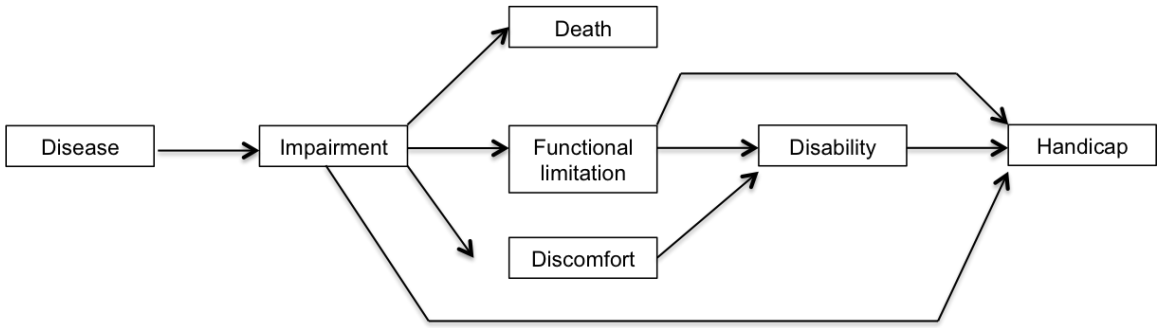

Figure 5.2. WHO 1980 conceptural model of disease impact.

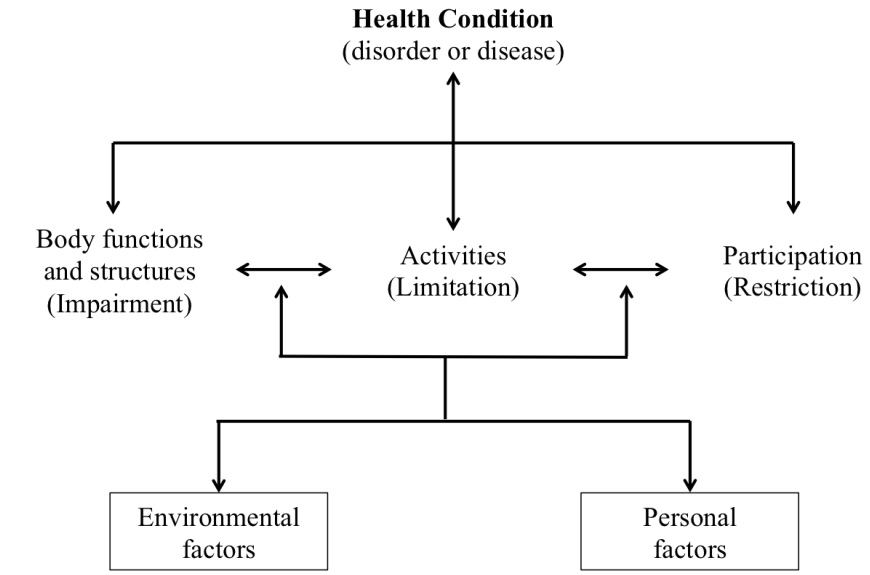

Figure 5.3. WHO 2001 conceptual model of disease impact

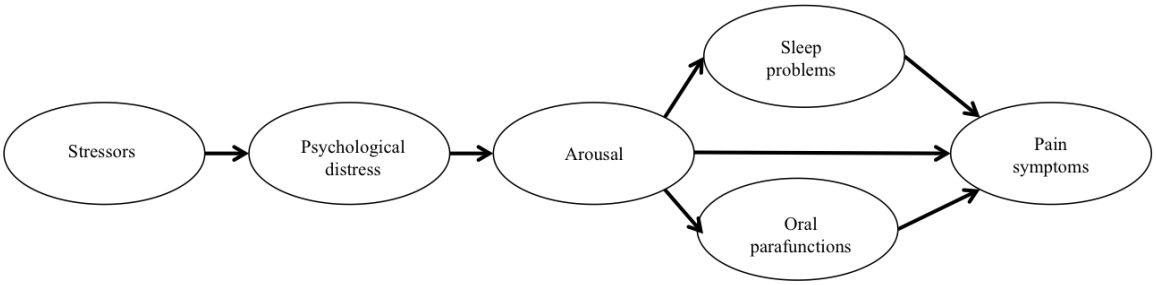

Figure 5.4. Structural model tested of factors predicting pain symptoms by Davis et al.

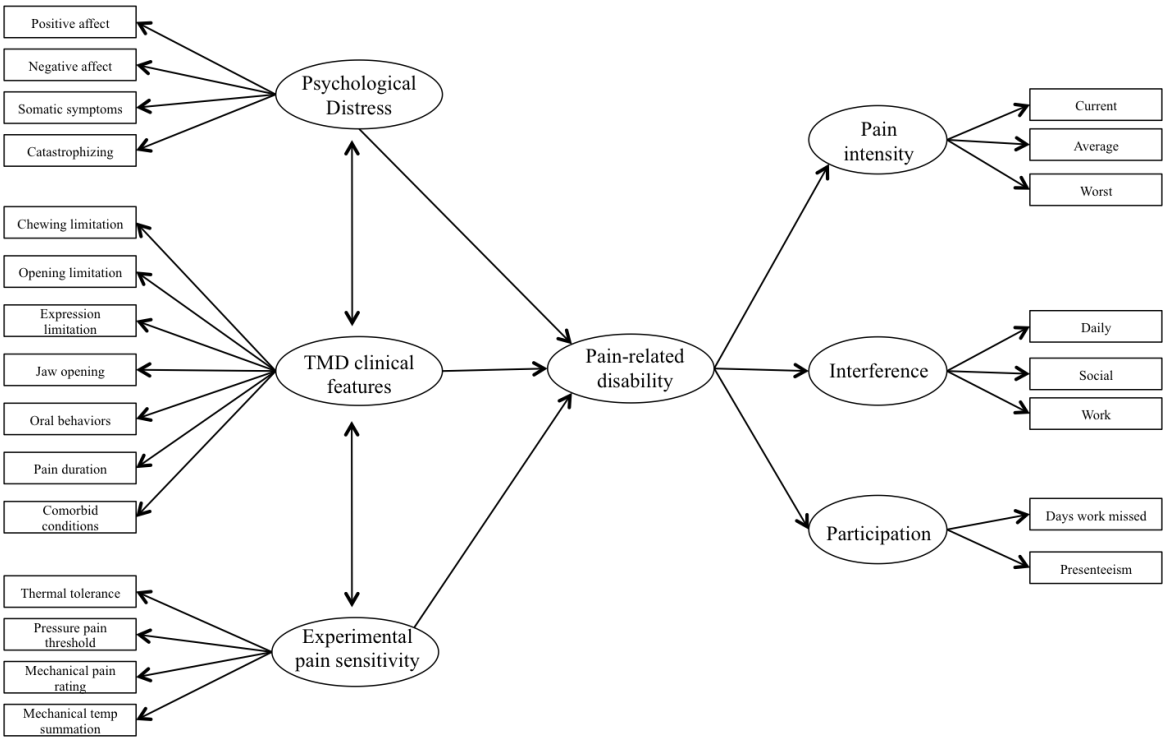

Figure 5.5. Hypothesized model of pain-related disability and constructs contributing to pain related disability

Latent variables are represented by circles while observed variables are shown as rectangles. Arrows from latent variables onto observed variables represent the variables used to create the latent construct. Arrows between latent variables represent hypothesized relationships to be tested.

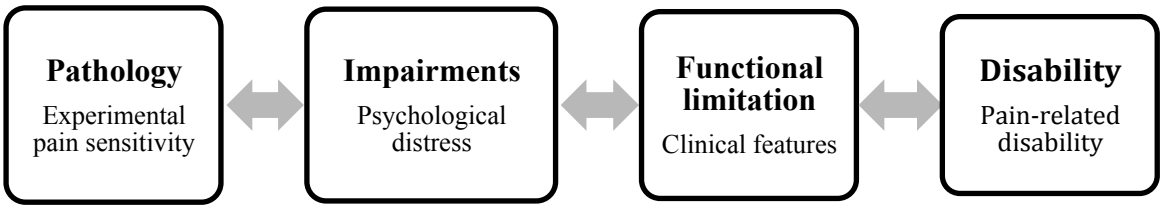

Figure 5.6. Nagi model modified using variables measured in the current study

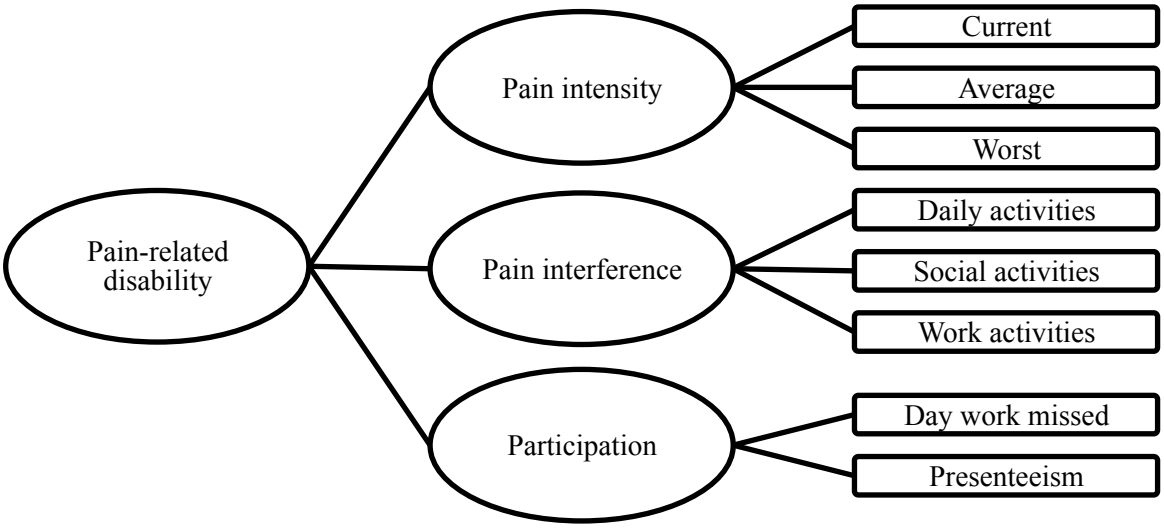

Figure 5.7. Structure of the second-order confirmatory analysis with latent variables denoting pain intensity, interference, and participation.
These three latent variables combine to comprise the latent variable of interest: pain-related disability.

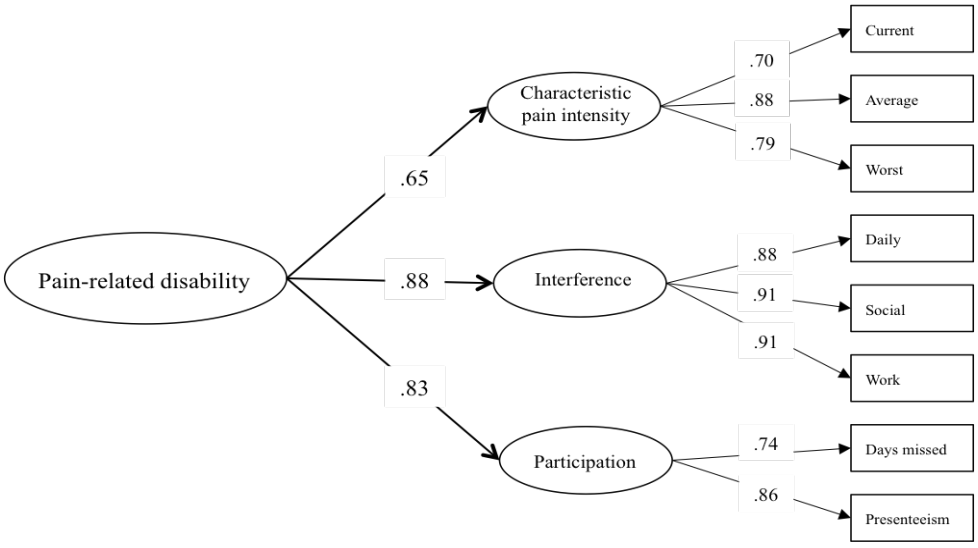

Figure 5.8. Re-validated structure of the Graded Chronic Pain Scale (GCPS) with the addition of the variable measuring presenteeism

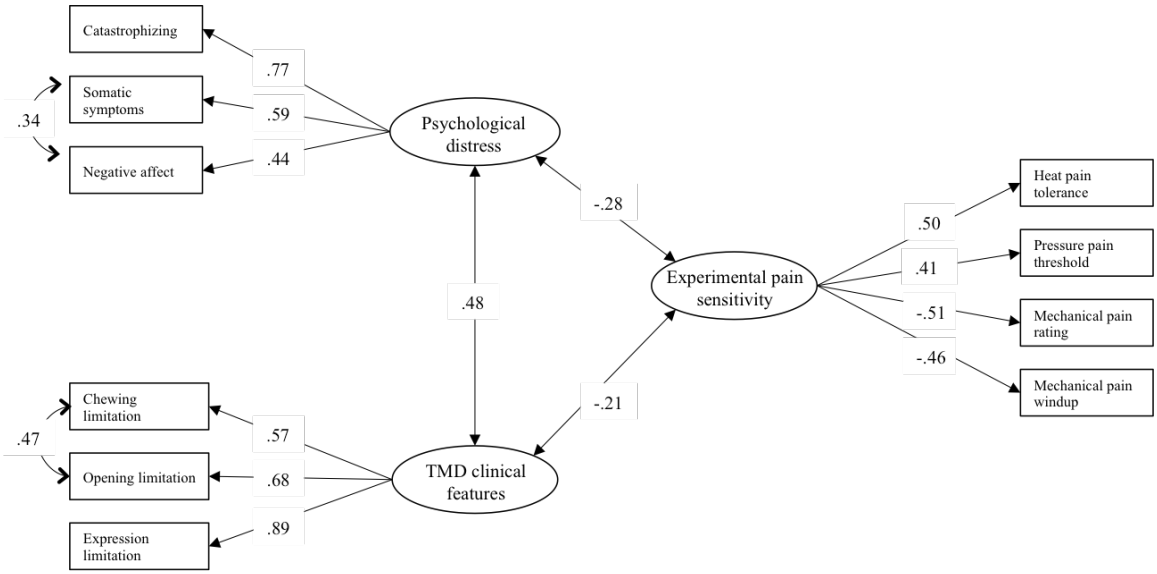

Figure 5.9. Measurement models of psychological features, jaw features, and experimental pain sensitivity

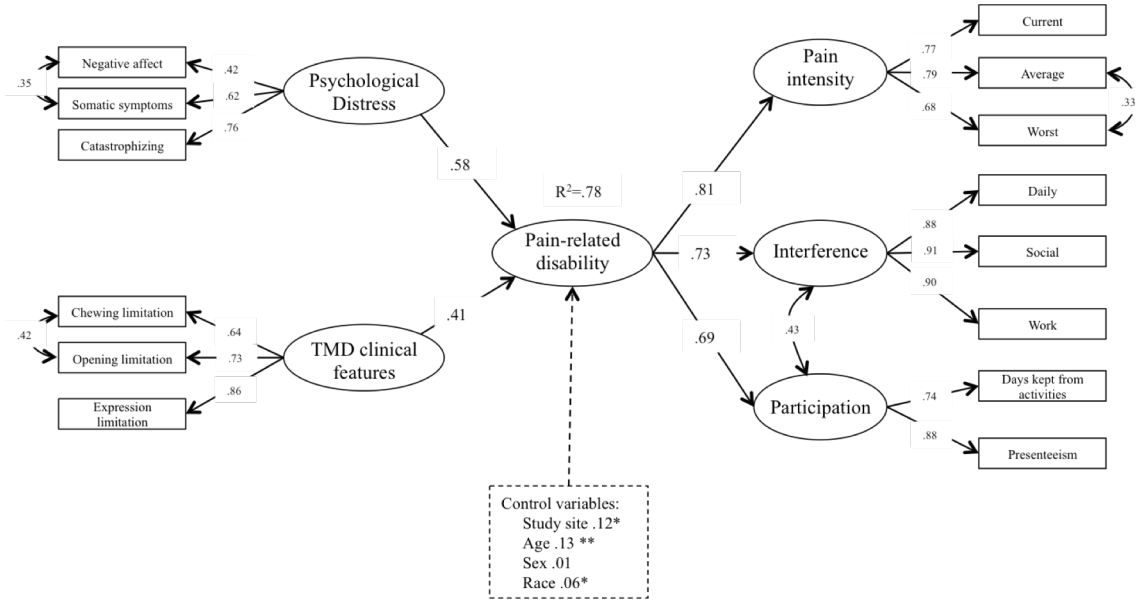

Figure 5.10. Final model and standardized parameter estimates of pain-related disability, psychological distress, and TMD clinical features.
Latent variables are shown in circles while observed variables are in rectangles. Control variables are shown surrounded by a dashed line. Curved arrows refer to covariance.
*p<.05 **p<0.001

Supplemental material

Mplus code used for final model

```
ANALYSIS:
ESTIMATOR=MLR;

MODEL:

   CPI BY CPI1 CPI2 CPI3;
   INTER BY I1 I2 I3;
   DIS BY DD1 DD2;
   PRD BY CPI INTER DIS;
   DIS WITH INTER;
   CPI2 WITH CPI3;

   JFLS BY JF1 JF2 JF3;
   JF1 WITH JF2;

   PD BY SOM CAT P8;
   SOM WITH P8

   PRD ON JFLS PD SITEID AGE SEX RACE;
```

Table 5.S.1. Correlation matrix among latent variables

	CPI	INT	DIS	PRD	JFLS	PD	Age
CPI							
INT	0.598*						
PAR	0.561*	0.718*					
PRD	0.814*	0.734*	0.689*				
JFLS	0.574*	0.518*	0.485*	0.705*			
PD	0.641*	0.579*	0.543*	0.788*	0.517*		
Age	0.116*	0.105*	0.098*	0.143*	0.000	0.000	

Note: CPI=Characteristic pain intensity, INT=Interference, PAR=Participation, PRD=Pain-related disability, JFLS=Jaw functional limitation score, PD=Psychological distress

*p<0.01 (two-tailed)

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CHAPTER SIX: SYNTHESIS

In this project I examined pain-related disability among people with chronic orofacial pain using two different approaches. The first approach determined characteristics associated with high pain-related disability using a binary logistic regression model to discriminate between people with low or high pain-related disability. The second approach explored the relationships between psychological distress, TMD clinical features, experimental pain sensitivity and pain-related disability using structural equation modeling. I hypothesized that increased psychological distress (including negative affect, somatization, and catastrophizing) and clinical features of TMD (such as as jaw limitation, oral behaviors, and pain upon palpation) along with greater sensitivity to experimental pain (reduced thermal pain tolerance and pressure pain thresholds, increased mechanical pain ratings) would be associated with increased pain-related disability. The broader goal was to provide insight into factors associated with pain-related disability for the purposes of increasing understanding the quality of life among people with chronic orofacial pain. Insight into these characteristics could help clinicians determine the risk of disability among patients with TMD, provide a template for exploring pain-related disability in other chronic pain conditions such as low back pain, and suggest targets for intervention to reduce disability.

Pain-related disability

Pain-related disability was assessed using the Graded Chronic Pain Scale (GCPS), which includes individual items addressing pain intensity, pain interference, and days kept from usual

activities. Each question is anchored to the previous 6 months. There is not an existing gold standard measure for evaluating pain-related disability, but the GCPS has been used in several chronic pain populations including TMD and we believe this to be a comprehensive measure of the impact of pain on the individual particularly with the addition of the variable measuring presenteeism. The latter conclusion was supported by findings that the addition of a variable measuring presenteeism as "how many days has your efficiency dropped below 50% of what you consider 'normal' for you because of facial pain?" increased the fit of a model of pain-related disability using the GCPS with and without the presenteeism variable (see further details below).

Predicting High Pain-related Disability: Summary of Findings

Aim one asked the question "how can we discriminate between people with low vs. high pain-related disability?" The results demonstrated that people with high pain-related disability had greater jaw functional limitation, more widespread body pain, and higher levels of catastrophizing compared to people with low pain-related disability. In contrast, experimental pain sensitivity, jaw opening, gender, and duration of pain did not increase the ability to discriminate level of disability. I created a final parsimonious model that included sociodemographic variables (age, sex, study site, and race/ethnicity) and the summary score from the Jaw Functional Limitation Scale, the catastrophizing subscale from the Coping Strategies Questionnaire, and the number of body sites reported as painful upon palpation during the clinical examination. This final model had a cross-validated AUC of 0.79, which was as good as the full model containing all variables, indicating good ability to discriminate between the two groups. The results cast light on the study's broader goals by identifying three features that can be used to identify treatment targets that are likely to influence the outcome of reduced pain-related disability.

Exploring Relationships Between Psychological, Clinical, and Experimental Measures and Pain-Related Disability: Summary of Findings

There were 3 major results in the work addressing aim 2. First, the good fit of the model of pain-related disability using the GCPS with the additional variable assessing presenteeism. Presenteeism was measured with the question "How many days has your efficiency dropped below 50% of what you consider normal?'. This question was combined with the variable assessing the number of days people were kept from activities and loaded onto a latent variable labeled "Participation". The resulting model demonstrated better fit than the model without the presenteeism variable. This finding supports the conclusion that among people with TMD, measuring presenteeism is a useful addition to the standard GCPS items. Second, measurement models for the constructs of interest: psychological distress, TMD clinical features, and experimental pain sensitivity were created and well fitting. Finally, the above results were combined in a full structural equation model. I developed a model involving regression of the latent variable measuring pain-related disability onto the two latent constructs that represented psychological distress (observed variables were negative affect, somatic symptoms, and catastrophizing) and TMD clinical features (based on observed variables from the JFLS measuring chewing limitation, opening and expression limitation). The model explained 78% of the variance in pain-related disability. The results indicated that increased psychological distress and increased jaw limitation were associated with increases in pain-related disability. The experimental pain sensitivity latent variable was dropped from analysis due to low parameter estimates that indicated a weak relationship between experimental pain sensitivity and disability. The results cast light on the study's broader goals by showing that jaw limitation, negative affect, somatic symptoms, and catastrophizing explain a large amount of variance in pain-related disability while experimental pain sensitivity did not.

Clinical and Public Health Significance

Several of our findings have significance for public health and how to address the burden of chronic pain. We found 33% of the community-dwelling study sample met criteria for high pain-related disability. This frequency of disability is concerning considering that one in twenty people in the general population have TMD symptoms and that high pain-related disability is associated with greater healthcare costs.[1]. The Institute of Medicine's report titled "Relieving Pain in America" includes people with TMD among the millions of Americans living with chronic pain[2].

The key result from both studies is that psychological distress and jaw functional limitation are associated with high pain-related disability among people with chronic orofacial pain. The clinical and public health implications of this finding underscore a need for assessment of both psychological distress and jaw limitation in TMD patients. This finding also supports a more comprehensive approach to the treatment of TMD, one that goes beyond the jaw and recognizes the whole person.

Psychological distress can be identified by self-report via questionnaires and can be targeted for intervention using cognitive behavior therapy (CBT) or biofeedback[3-5]. Research has shown a decrease in pain-related disability at least in the short term after CBT and biofeedback interventions. Jaw functional limitation can be assessed in a 10-minute self-report questionnaire, and may be targeted with physical therapy to increase an individual's ability to open and chew[6, 7] and increase physical activity[8] to reduce pain-related disability.

Interestingly, we found that sex and pain duration were not associated with disability, conflicting with previous research that indicated women were more likely to experience pain-

related disability. Our finding suggests that disability is as common among men as women while women are still more likely to suffer from chronic TMD.

Experimental pain sensitivity was assessed as a measure of underlying biological pathology (a construct in Nagi's model of disability) and not found to be associated with pain-related disability. Based on this finding, we can conclude that experimental pain sensitivity is not an adequate marker of biological pathology. We should not rule out the presence of an underlying biological pathology contributing to pain-related disability, but instead focus on the more proximal causes such as pain coping strategies and psychological dysfunction.

Conclusions

Findings from the two approaches had more commonalities than differences. Both approaches identified jaw functional limitation, somatic symptoms, and catastrophizing as key contributors to pain-related disability. After accounting for those measures, experimental pain sensitivity did not meaningfully contribute further to pain-related disability, a result that was seen using both approaches. Likewise, results from both studies indicated neither gender nor duration of pain symptoms contributed additionally to pain-related disability, a finding that contradicts previous research. I think this means high impact is the result of individual level psychological and social conditions and less likely to be rooted in biological or hormonal causes. These results are relevant to the study's broader goals of assessing the importance of factors (including established risk factors for pain onset or pain severity) to understanding the impact of pain.

However, the two approaches revealed some important differences in the types of factors that, on the one hand discriminate between high- and low-disability, and on the other hand, explain relationships among correlates of disability. For example, using SEM, the number of

body pain sites displayed poor model fit and hence was not retained in the final model whereas this variable was useful in discriminating between low and high pain-related disability in the results of aim one. This could mean the number of body sites is not predictive of pain impact or it may point to an error in methodology. I hypothesized painful sites would load onto the variable representing TMD clinical features but upon further consideration I think whole body pain may be a separate construct deserving it's own measurement. I am hesitant to disregard the importance of body pain sites for two reasons: 1) the established relationship between psychological distress and body pain and 2) the discriminatory importance of number of pain sites found in the aim one results. Likewise, somatization score was not included in the final model addressing aim one because somatization did not contribute to a difference in the AUC, but somatization was included in the conceptual model tested in aim two and shown to significantly load onto the psychological distress variable. These differences in findings revealed by the two approaches are not easy to explain. I interpret these discrepancies in part due to the nature of the methods used and potential relationship between somatic symptoms and widespread body pain measured by palpation of body sites. The logistic model used to address aim 1 involved each variable controlled for the other variables in the model whereas the SEM approach did not involve adjustment for other variables but accounted for measurement error.

It is important to note the limitation of the cross-sectional setting for drawing conclusions about causality between these factors identified and increased pain-related disability. Without following people over time to measure the incidence of pain-related disability it is not possible to draw substantial conclusions about the causes or risk factors of disability.

The use of cross-sectional data proved necessary for testing our theoretical model of existing pain-related disability to utilize a large sample size for exploration of a variety of

variables. Examining the experience of people who had been living with chronic pain for multiple years and have had time to develop coping strategies and experience the impact of their condition on their work, social, and family obligations, permitted the conclusion that psychological distress and jaw functional limitation are key areas of concern related to disability. These findings also support the conclusion that duration of pain, sex, and experimental pain sensitivity are not central to understanding pain-related disability among people with chronic orofacial pain. I surmise that the experience of people with acute pain or recently developed chronic pain (at 6 months) may differ.

Future Research

There are several next steps to further inform clinicians and researchers in the area of pain-related disability. Primarily, researchers can confirm the relationship reported here by measuring these factors in a longitudinal study design. The OPPERA study included a prospective study of 3,258 people who were pain-free at enrollment and 208 people developed TMD symptoms. Analysis examining baseline measures of the same variables measured in this project and measures repeated at onset of symptoms would provide insight into the relationship between factors identified here and the onset of pain-related disability. In future cohort studies, measuring pain-related disability, psychological distress and jaw functional limitation at multiple time points would allow for conclusions about how these factors influence one another and fluctuate over time.

Beyond these tasks, intervention studies attempting to reduce pain-related disability should explore interventions on the factors identified in this research. Measuring and targeting features associated with pain-related disability can be accomplished in the clinical and research

setting and should be a priority for interventions in order to reduce the public health burden of chronic pain.

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